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United States
Environmental Protection Agency

Office of Chemical Safety
and Pollution Prevention

Integrated Risk Assessment for Chevron Waste Plastic Fuels

(P-21-0144, 145, 146, 147, 148, 149, 150, 152, 153, 154, 155, 156, 157, 158, 160, 161, 162, and 163)

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[**P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163**]

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[redacted]

1 SUMMARY

1.1 Background

Chevron Corporation submitted premanufacture notices (PMN) for eighteen waste plastic fuel streams, P-21-0144 through 0150, P-21-0152 through, and P-21-0160 through 0163). These new chemical substances (NCSs) are complex mixtures. They are manufactured concurrently with petroleum streams and have identical composition; the only difference is that the feedstocks are waste plastic-based sources rather than petroleum-based sources. The intended uses are as fuels, fuel components, and chemical intermediates or refinery feedstocks.

This document provides a review by the New Chemicals Division (NCD) in the U.S. EPA Office of Pollution Prevention and Toxics (OPPT) of the chemistry, environmental fate, environmental release, hazard (environmental and human health), and exposure (occupational, general population, consumer and aquatic organisms) to assess the potential risk of the NCSs to human health and the environment.

In addition, NCD is using a tiered approach for information to evaluate renewable and other, non-petroleum-based sources used as a fuel blend under the Toxic Substances Control Act (TSCA). Consistent with EPA guidelines on mixture assessment, when data for the mixture of concern (Tier 1) or toxicologically similar/ analogous mixtures (Tier 2) are unavailable, the use of Tier 3 or Tier 4 is used. This hierarchical approach is summarized below and additional details can be found in Appendices A and D.

Tier 1: Experimentally-derived data on the new chemical substance.

Tier 2: Experimentally-derived data on an analogous mixture.

Considerations for whether an analogous mixture is appropriate include: carbon chain length; paraffinic, isoparaffinic, olefinic, naphthenic, and aromatic (PIONA) composition; and physical-chemical properties (*e.g.,* physical state, boiling point, melting point, vapor pressure).

Other considerations include whether there are available data on representative constituents and/or constituents that will be the primary drivers of human health or environmental hazards. Data from this tier may be combined with data from Tier 3 to ensure that the resulting assessment protects human health and the environment and is based on the most reliable data available.

Tier 3- Experimentally-derived data on the most prevalent and/or most toxic constituents of the new chemical substance (human health hazard and environmental fate).

Tier 3- Predicted (*in silico*) data on all constituents combinedusing the Toxic Unit approach (environmental hazard). The Toxic Unit approach, which predicts ecotoxicity endpoints for a mixture by combining the toxic contributions from each constituent, is provided in Appendix D.

[redacted]

Tier 4- Predicted (*in silico*) data on most prevalent constituents if no experimentally-derived data are available. Predictive tools (*e.g.,* EPISuite) will be used to fill data gaps for physical-chemical and environmental fate properties and other tools (e.g., OECD QSAR Toolbox) will be used for human health hazard.

Tier 4- Use of the most toxic individual constituents,based on either experimental data an/or predictions (*i.e.,* ECOSAR) and conservative assumptions in a screening-level assessment when mixture characterization is inadequate for higher tiered assessment (environmental hazard).

1.2 Chemistry

Fuel streams such as these NCSs are comprised of dozens of different paraffinic (isoparaffinic), naphthenic, olefinic, and aromatic molecules (P[I]ONA), which makes determining their chemical makeup challenging. In addition, the composition of these substances is variable since the fuels are defined using physical properties such as boiling point rather than their precise chemical makeup. However, the composition of these substances can be estimated using gas chromatography techniques to measure their P(I)ONA profile, which describes the relative concentrations of the different types of hydrocarbon within a given fuel stream (some measurements do not distinguish between paraffinic and isoparaffinic hydrocarbons). Chevron has provided some compositional data for of the petroleum analogues, which can also be used as an approximation for the chemical makeup of the NCSs.

1.3 Environmental Persistence and Bioaccumulation Potential

Using the persistence (P) and bioaccumulation (B) rating system described in Section 3, NCD estimated that two of the 18 NCSs could have a limited persistence ("P1") potential (P-21-0162 and 0163). The remaining 16 are estimated to range from from limited to very persistent ("P1-P3") potential. Five of the 18 NCSs are estimated to have a low potential for bioaccumulation ("B1") (P-21-0146, 0160, 0161, 0162 and 0163), three of the mixtures have a low to moderate potential for bioaccumulation ("B1-B2") (P-21-0147, 0148 and 0150), and the remaining 10 are estimated to have a range of from low to high potential for bioaccumulation ("B1-B3") .

Overall, the new chemical substances have the potential to bioaccumulate and be persistent in the environment, such that repeated exposures may cause food-chain effects via accumulation in exposed organisms.

1.4 Environmental and Human Health Hazards

For environmental hazard, the eighteen waste plastic NCSs were assessed with a four-tier approach that incorporated whole fuel-stream and hydrocarbon constituent data. Nine of the NCSs, P-21-0145, P-21-0146, P-21-0147, P-21-0148, P-21-0149, P-21-0150, P-21-0155, P-21-0156, and P-21-0158, were evaluated using acceptable hazard data from four analogous fuel streams (Tier 2). The other nine used individual constituent hazard information and combined them using the toxic unit approach, which predicts ecotoxicity endpoints for a mixture by combining the toxic contributions from each constituent. Seven NCSs (P-21-0147, P-21-0148, P-21-0150, P-21-0160, P-21-0161, P-21-0162, and P-21-0163) were classified as a moderate environmental hazard. Eleven NCSs (P-21-0144, P-21-0145, P-21-0146, P-21-0149, P-21-0152, P-21-0153, P-21-0154, P-21-0155, P-21-0156, P-21-0157, and P-21-0158) were classified as a high environmental hazard.

[redacted]

For human health hazard, , NCD identified skin and eye irritation; acute toxicity; systemic toxicity (neurotoxicity, body weight effects, and liver, kidney, blood, spleen, and other organ effects); reproductive and developmental toxicity; oral and inhalation portal of entry effects; genetic toxicity; and carcinogenicity as hazards of the NCSs based on Tier 2 analogous mixtures and Tier 3 constituents of the NCSs. EPA identified hydrocarbon pneumonia/ aspiration hazard based on the chemical composition (petroleum). The U.S. EPA assumes that respiratory tract irritation is possible when exposed to the NCSs. For the quantitative risk assessment, NCD used a combination of Tier 2 analogous stream information and Tier 3 worst-case constituent information, depending on the available information for the oral, inhalation and dermal routes of exposure.

1.5 Environmental Releases and Exposure

The NCSs are domestically manufactured and used as fuels, fuel components, and chemical intermediates/refinery feedstocks. Three main scenarios are assessed: manufacturing, processing and use. The activities assessed under these scenarios are specific to the individual NCSs, but may include:

- *Manufacturing:* NCD assessed environmental releases from volatilization. Inhalation exposure to workers was assessed for various activities throughout the refinery . Dermal exposure was assessed for workers sampling the liquid product and loading liquid product into tank trucks.
- *Processing:* NCD assessed releases from blending and loading at bulk terminals. Inhalation exposure to workers was assessed for the following activities: worker inhalation exposure, loading liquid product into tank trucks, tank standing/working losses, sampling liquid product, and fugitive emissions from the process. Dermal exposure was assessed for workers loading liquid product into tank trucks and unloading liquid raw material from tank trucks.
- *Use:* NCD assessed releases from fuel and chemical intermediate uses. Inhalation and dermal exposure to workers was assessed for unloading liquid raw materials from tank trucks.

Exposure to the general population was assessed for the following exposure pathways from manufacturing, processing and use releases to air, water and landfill: drinking water, fish ingestion, groundwater impacted by landfill leachate, and inhalation of stack/fugitive air. Exposure to consumers was assessed via dermal contact.

1.6 Risk Conclusions

There were no environmental risks to aquatic organisms from the manufacturing of the 18 NCSs as there were no expected releases to water. Environmental risks to aquatic organisms from acute exposures during processing were identified for P-21-0144, 0145, 0146, 0147, 0149, and 0150 because the estimated surface water concentrations exceeded the acute concentrations of concern. Environmental risks to aquatic organisms from acute exposures during use were identified for P-21-0155, 0156, 0157, and 0158 because the estimated surface water concentrations exceeded the acute concentrations of concern. Environmental risks to aquatic organisms from acute exposures during both processing and use were identified for P-21-0148 and 0152 because

[redacted]

the estimated surface water concentrations exceeded the acute concentrations of concern. Environmental risks to aquatic organisms from acute exposures were not identified for P-21-0153, 0154, 0160, 0161, 0162, or 0163 as there were no expected releases to water. Environmental risks to aquatic organisms from chronic exposure were not identified.

Human health risks for systemic effects were identified for worker inhalation exposures to P-21-0144, P-21-0146, P-21-0148, P-21-0152, P-21-0154, P-21-0155, P-21-0156, and P-21-0157. Risks were identified workers for systemic effects via dermal contact to P-21-0152, P-21-0153, P-21-0154, P-21-0155, and P-21-0156. For workers, cancer risk estimates from inhalation exposure ranged between 5.1E-08 and 7.1E-03. Hazards for irritation to the respiratory tract (all cases), skin (all cases except P-21-0152, P-21-0162, and P-21-0163), and eye (all except P-21-0154) via inhalation and dermal contact were also identified for workers. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards.

For P-21-0144, 0148, 0149, 0150, 0152, and 0157, risks were identified for the general population (infants) for systemic and/or oral portal-of-entry effects via drinking water. Risks to adults for this exposure route were identified for P-21-0152. For P-21-0145, 0146, 0147, 0155, 0156, and 0158, risks were not identified for the general population for systemic and/or oral portal-of-entry effects via drinking water (adults or infants). For P-21-0153, 0154, 0160, 0161, 0162, and 0163, risks to the general population via drinking water were not evaluated because releases to surface water are not expected.

For P-21-0144, 0148, 0149, 0150, 0152, 0155, 0156, 0157, and 0158, risks were identified for the general population for systemic and/or oral portal-of-entry effects via fish ingestion.
For P-21-0146 and 0147, risks were not identified for the general population for systemic and/or oral portal-of-entry effects via fish ingestion. For P-21-0153, 0154, 0160, 0161, 0162, and 0163, risks to the general population via fish ingestion were not evaluated because releases to surface water are not expected.

For P-21-0144, 0145, 0146, 0147, 0148, 0149, 0150, 0156, 0157, and 0158, risks were not identified for the general population for systemic and/or oral portal-of-entry effects via intake of groundwater impacted by landfill leachate. For P-21-0152, 0153, 0154, 0155, 0160, 0161, 0162, and 0163, risks to the general population via groundwater impacted by landfill leachate were not evaluated because releases to landfill were expected to be negligible (below modeling thresholds) or no releases are expected.

For P-21-0148, 0152, 0154, 0155, 0156, 0157 and 0158, risks were identified for the general population for systemic and/or inhalation portal-of-entry effects via fugitive air inhalation. For P-21-0144, 0145, 0146, 0147, 0149, 0150, 0160, 0161, 0162, and 0163, risks were not identified for the general population for systemic and/or inhalation portal-of-entry effects via fugitive air inhalation. For P-21-0153, there is insufficient information to assess hazard because of a lack of suitable Tier 2 mixtures or representative constituents with inhalation PODs. Therefore, EPA cannot make a risk determination for the general population exposed via fugitive air inhalation.

[redacted]

For P-21-0149, 0152, 0155, 0156, 0157 and 0158, risks were identified for the general population for systemic and/or inhalation portal-of-entry effects via stack air inhalation. For the remaining cases, risks to the general population via stack air inhalation were not evaluated because no releases are expected

For the general population, cancer risk estimates for drinking water ranged between 1.3 E-10 (P-21-0146) and 1.7E-08 (P-21-0148). The cancer risk estimates for fish ingestion ranged between 7.8E-10 (P-21-0146) and 3.3E-05 (P-21-0158). The cancer risk estimates for consumption of groundwater impacted by landfill ranged between 2.7E-09 (P-21-0144) and 1.8E-07 (P-21-0148). The cancer risk estimates for inhalation of fugitive air ranged between 8.3E-8 (P-21-0144) and 1.2E-04 (P-21-0150). The cancer risk estimate for inhalation of stack air for P-21-0158 was 2.5E-01.

Consumer uses were identified for P-21-0144, 0145, 0146, 0147, 0148, 0149, 0150, 0155, 0156, 0157, and 0158. Consumer uses were not identified for the remaining cases. Non-cancer risks to consumers via dermal contact were identified for P-21-0155 and not identified for any of the remaining cases. Hazards for respiratory, dermal, and eye irritation via dermal contact were identified for consumers. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards.

1.7 Assumptions and Uncertainties

Information submitted for the NCSs included only a few physical/chemical properties and general chemical composition information. The constituents of the new chemical substance mixtures were not reported. The lack of chemical constituent information and approximate weight fraction for each introduces uncertainties in the understanding of the chemical composition of the NCSs. Furthermore, the process used to manufacture the NCSs will likely result in mixtures of varying composition. This adds a level of uncertainty to predictions of toxicity based on mixture composition, or when reading across from another fuel stream of variable composition. In addition, as complex mixtures, there is uncertainty regarding the physical/chemical properties of the NCSs and only limited information was supplied by the submitter.

The assessments for environmental hazard and risk, and human health hazard and risk are based on available information for Tier 2 analogous mixtures and information on constituents (Tier 3). The assessment for environmental fate used a weight of evidence approach using information from Tiers 2, 3, and 4. In addition, potential degradation products of the new chemical substance were not evaluated because NCD does not have adequate information to predict degradation products. Information on analogous mixtures (Tier 2) may not adequately represent the new chemical substance, and information on individual constituents (Tier 3) will not reflect potential synergistic, antagonistic, or other interactions arising from the presence of multiple constituents within a mixture. Tier 4 information is based on prediction models and introduces more uncertainty into its use.

Where chemical-specific or site-specific information is not available, NCD used estimation methods and modeling approaches to estimate release and exposure, and applies engineering judgment where appropriate. There is some level of uncertainty associated with each method or model, including the use of surrogate monitoring data to assess inhalation exposure to truck drivers.

[redacted]

For the consumer exposure estimates, dermal exposure estimates were developed. The lack of consumer inhalation modeling for gasoline dispensing introduces an uncertainty resulting in an underestimation of the total exposure to consumers.

For cancer inhalation risks for the general population, NCD used an average annual air concentration when calculating the lifetime average daily dose (LADD) estimate and assumed exposure to that concentration throughout the lifetime. The use of this assumption would overestimate risks to individuals who spend less than a lifetime at the affected location.

1.8 Potentially Useful Information

- Skin Irritation
- Eye Irritation
- Respiratory depression/irritation
- Hydrocarbon pneumonia/aspiration hazard
- Reproductive developmental toxicity
- Systemic toxicity
- Genetic toxicity
- Carcinogenicity
- Aquatic Toxicity
- Consumer inhalation exposures at gas stations

2 CHEMISTRY

The 18 fuel streams described in this report are complex UVCB[1] substances that are derived from waste-plastic (WP) feedstocks that are comprised of [redacted] These next-generation fuel streams are manufactured concurrently with their petroleum counterparts as inseparable mixtures which are then used as blending stocks for various fuels (*e.g.,* jet, diesel, gasoline, etc.), or as a chemical intermediate in their production. While [redacted]% of the WP feedstock has been used to synthesize these substances on a pilot scale, Chevron plans to start producing these substances commercially using [redacted]% of the WP feedstock and gradually increase the relative concentration of the WP feedstock to [redacted]%. Chevron expects to reach the max target ([redacted]%) in the next 10+ years.

The NCSs are often obtained by [redacted]. Though they may have divergent downstream processing [redacted] all the NCSs originate from [redacted] reaction pathways. These pathways are distinguished by the point in the refinement process where the [redacted]. The NCSs are formed when [redacted] Alternatively, some NCSs can be obtained [redacted]. (Note: Information obtained from the "processing" document provided by Chevron)

[1] UVCB = unknown or variable composition, complex reaction products and biological materials

[redacted]

Some of the steps in the refinement process utilize [redacted]

Therefore, compositional data and physical/chemical properties can only be obtained for the WP/petroleum mixture and not the NCS alone.

Chemical Composition:

Fuel streams such as these NCSs are comprised of dozens of different paraffinic (isoparaffinic), naphthenic, olefinic, and aromatic (P[I]ONA) molecules, which makes determining their chemical makeup challenging. In addition, the composition of these substances is variable since the fuels are defined using physical properties such as boiling point rather than their precise chemical makeup. However, the composition of these substances can be estimated using gas chromatography techniques to measure their P(I)ONA profile, which describes the relative concentrations of the different types of hydrocarbon within a given fuel stream (some measurements do not distinguish between paraffinic and isoparaffinic hydrocarbons).

Chevron claims that the WP-derived fuels are chemically equivalent to their petroleum analogues. In order to establish this equivalency, they used a pilot plant to measure the P(I)ONA profiles of the reaction products produced when the WP/petroleum feedstocks are treated using [redacted] processes, see Figures 1 and 2, respectively. The P(I)ONA profiles were measured after the reaction products were separated into various ranges via [redacted] (*e.g.,* gasoline, jet, diesel, etc.).(Note: [redacted])

[redacted]

Table 1. General Properties of PMN Substances and their Corresponding Petroleum Analogues

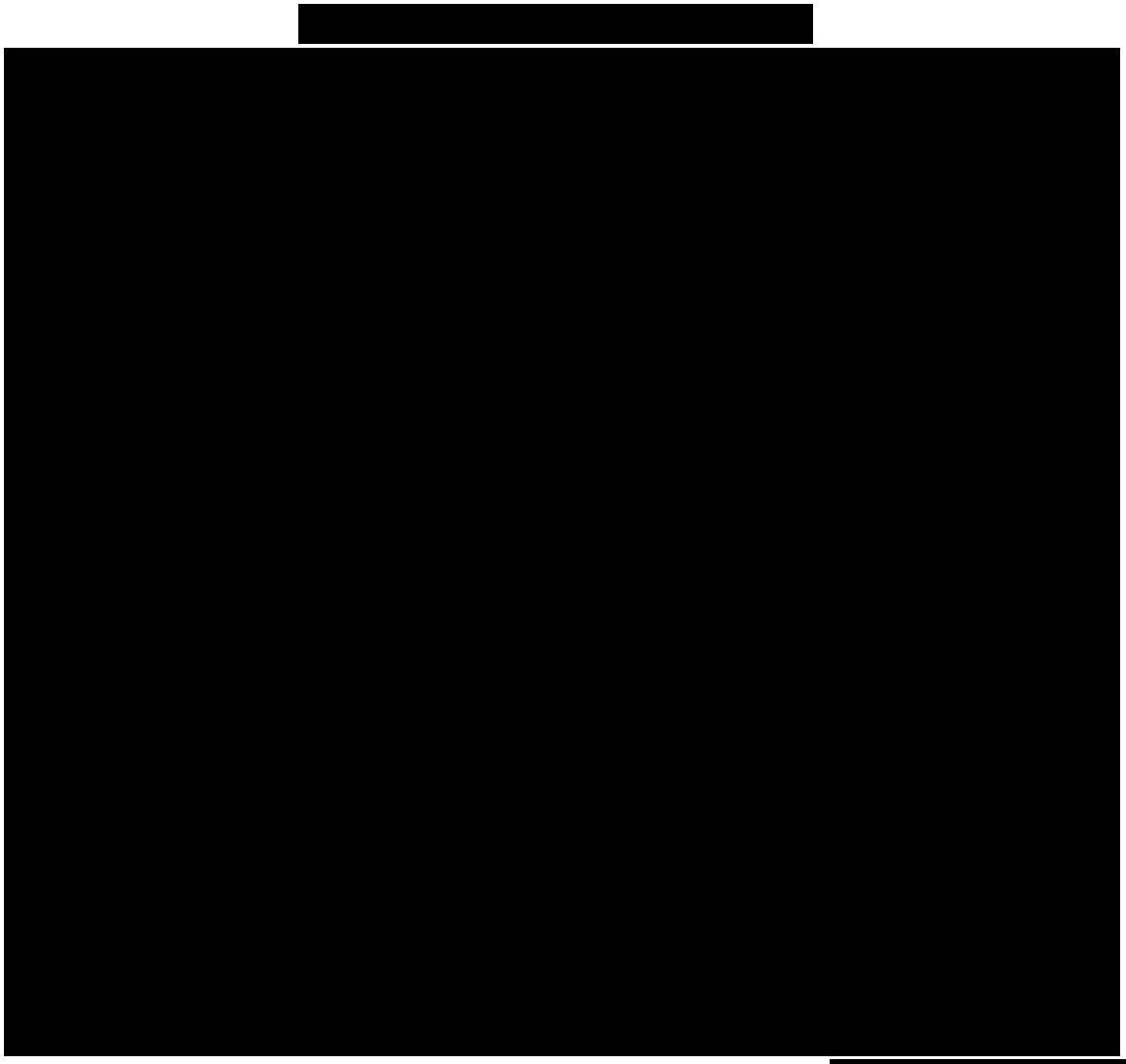

Figure 1. Concentration effects of WP feedstocks on the composition of processed fuels. Graphic representation of PIONA profile for and P(I)ONA profile for the gasoline, jet, and diesel cuts (b). Information provided by Chevron in attachment "PO_Chemical_Composition_2021-5-20" (Note:)

Inspection of the data for shows that, in general, there is no significant variation in the P(I)ONA profile for each range despite increasing amounts of WP feedstock (Figure 1). Although, increasing the concentration of WP feedstock to % does impact the content relative to . Given that there is very little variation overall, it is reasonable to conclude that the concentration of WP feedstock (up to %) does not significantly change the composition of the products. (Note:)

Figure 2. Concentration effects of WP feedstocks on the composition of (Fluid Catalytic Cracking) FCC processed fuels separated into gasoline, jet, and diesel cuts. Information provided by Chevron in attachment "PO_Chemical_Composition_2021-5-20" (Note: Plastic Oil #2 and #3 are different WP feedstocks. No compositional or processing information was provided for these substances)

To test concentration effects on the , Chevron varied the relative concentration of petroleum and WP feedstocks such that % WP feedstock was used (Figure 2). For this study, multiple WP feedstocks were tested (Plastic oil #2, Plastic oil #3 in Figure 2). Like the results for the , very little variation in the P(I)ONA profiles was observed as the concentration of the waste plastic feedstock was increased to %. However, when % of the WP feedstock was used, variation did occur. Despite these differences, Chevron plans to use % feedstock when manufacturing these substances. The PONA profiles measured for the gas, jet, and diesel ranges do not show significant variation at % waste plastic feedstock was used, which suggests that the concentration of these PMN substances would not significantly change when % WP feedstock is used. This supports Chevron's claim.

Chevron has provided some compositional data for the petroleum analogues, which can also be used as an approximation for the chemical makeup of the NCSs. Initial characterization was done by measuring their P(I)ONA profiles (Table 2). Inspection of the data shows that it is consistent with the definitions contained in the chemical IDs associated with the petroleum analogues.

The composition of the petroleum analogues was further characterized by measuring or calculating the major components that comprise each hydrocarbon category (*i.e.,* paraffinic, isoparaffinic, olefinic, etc.). These substances were determined using four different techniques including

[redacted] In all cases, the data (not shown in this report, but submitted by Chevron[2]) showed a normal distribution of compounds by carbon number within a group type. For samples that were not available for measurement, this distribution behavior was used to estimate the most abundant compounds in the sample.

Comparing the applicable experimental conditions of these methods with the physical properties of the petroleum analogues, it is clear that multiple methods may be required to estimate their composition. However, Chevron has not specified which characterization method was used to determine the composition of the petroleum analogues. They also have not indicated what information was obtained using the distribution within a hydrocarbon category (*i.e.,* not directly measured). The percentages associated with the major components are relative to the entire PMN substance and not respective to the individual category (Table 2).

Table 2. Percent Compositional Information for Petroleum Analogues

Case	Name	CASRN
P-21-0144	[redacted]	
	Major Products:	
P-21-0145	[redacted]	
	Major Products:	
P-21-0146	[redacted]	
	Major Products:	

[2] This raw data was never provided, but Chevron made this claim in the document "Analytical Methods for Composition Data Collection_2021-8-13"

[redacted]

Table 2. Percent Compositional Information for Petroleum Analogues

Case	Name	CASRN	[redacted]
P-21-0147	[redacted]		
	Major Products:		
P-21-0148	[redacted]		
	Major Products:		
P-21-0149	[redacted]		
	Major Products:		
P-21-0150	[redacted]		
	Major Products:		
P-21-0152	[redacted]		
	Major Products:		
P-21-0153	[redacted]		
	Major Products:		
P-21-0154	[redacted]		

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table 2. Percent Compositional Information for [redacted] Analogues

Case	Name	CASRN	[redacted]
	[redacted]		
	Major Products:		
P-21-0155	[redacted]		
	Major Products:		
P-21-0156	[redacted]		
	Major Products:		
P-21-0157	[redacted]		
	Major Products:		
P-21-0158	[redacted]		
	Major Products:		
P-21-0160	[redacted]		
	Major Products:		
P-21-0161	[redacted]		
	Major Products:		
P-21-0162	[redacted]		
	Major Products:		
P-21-0163	[redacted]		

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table 2. Percent Compositional Information for [redacted] Analogues		
Case	Name	CASRN
	[redacted]	
Major Products:	[redacted]	

Physical/Chemical Properties:

The NCSs are produced concurrently with their petroleum analogues as an inseparable mixture and it is impossible to measure the physical/chemical properties of the WP-derived fuels by themselves. Therefore, the company provided information concerning the WP/petroleum mixture and petroleum analogues (Table 3). Data concerning the petroleum analogues was also augmented with values from a variety of different sources that are indicated in the table caption. Table 3 contains both measured and computed data. All liquid substances in Table 3 are soluble in hydrocarbon solvents. Some of the submitted vapor pressure data for the NCSs appear to be in error (see footnote "c" in Table 3) given the other physical characteristic provided in the definition of the PMN substance. These substances and the petroleum analogues are UVCB materials. Any measured data on any given substance is dependent upon the composition of the substance analyzed. Therefore, the values should be considered approximate and not absolute.

[redacted]

Table 3. Physical/Chemical Properties of Waste-Plastic/Petroleum Mixtures and Petroleum-Only Analogues

[redacted]

[a]Taken from definition unless otherwise indicated; [b]data submitted with PMN and measured at 37.5 °C; [c]The submitted values do not make sense given the other physical properties; [d]Data submitted by company unless otherwise indicated; [e]Data submitted by company with no experimental details; [e]Data for this substance taken from Screening Level Hazard Characterization - Gasoline Blending Streams Category unless otherwise indicated; [f]Data for this substance taken from HPV Gasoline Blending Streams Hazard Characterization unless otherwise indicated; [g]Measured for high/low MW species; [h]Exp./Est.; [i]Taken from definition; [j]Data taken from the Chemistry Report for the Glyceridic-derived fuel streams submitted by Chevron; [k]Lubricating Oils Category documents found at the API HPV

[redacted]

2.1 Use Information

The NCSs are intended to be used as fuels/fuel components and as chemical intermediates/refinery feedstocks. The NCSs are manufactured concurrently with petroleum mixtures and the submitter claims that they have identical compositions, with the only difference that the feedstocks for the NCSs are waste plastic-based sources rather than petroleum-based sources.

2.2 Identification of Available Information for Tiered Approach to Fate, Hazard, and Risk Evaluation

The submitter did not provide any experimentally derived hazard (including environmental fate) information on the NCSs. This would be Tier 1 information and be the most relevant to evaluate the hazard and fate properties of a mixture.

NCD used a combination of Tier 2, 3 and 4 information to assess the environmental fate and transport, hazard and risk evaluation for the NCSs. Tier 2 information is based on identifying and using information from a sufficiently similar or analogous mixture, which can be used to read-across to the new chemical substance. If an analogous mixture cannot be found, Tier 3 information is based on information available for constituents of the mixture. Tier 4 (the final Tier in the approach) uses modeled or estimated information based on constituents.

NCD used Tier 2 information for the following analogous mixtures based on structural similarity (carbon chain length and PIONA profile) and availability of relevant fate or hazard information for read across:

- 64741-41-9
- 64741-54-4
- 64741-55-5
- 64741-59-9
- 64741-62-4
- 64741-66-8
- 64741-68-0
- 64741-77-1
- 64741-78-2
- 64742-05-8
- 64742-47-8
- 64742-48-9
- 68334-30-5
- Commercial hexane (no CASRN)
- Isobutane/2-methylbutane mixture (50:50)
- Stoddard Solvent IIC (64742-88-7)
- White mineral oil (no CASRN)

[redacted]

Tier 3 information was used in both the environmental fate and environmental and human health hazard/risk evaluations, and when pertinent, it was used with Tier 2 information in a weight-of-the-evidence approach. Model estimations (Tier 4 information) were also used in the environmental fate assessment to evaluate persistence and bioaccumulation and in environmental hazard assessment.

3 ENVIRONMENTAL FATE AND TRANSPORT

Environmental fate is the determination of which environmental compartment(s) a chemical moves to, the expected residence time in the environmental compartment(s), and the known or expected removal and degradation processes. Environmental fate is an important factor in determining exposure and risk. U.S. EPA has a Persistent, Bioaccumulative and Toxicity (PBT) policy established in 1999 that uses a simple scoring system for persistence, bioaccumulation and toxicity. Persistence is important because chemicals that are not degraded in the environment will persist and may buildup in the environment, and thus increase potential for exposure. Persistence scores are, going from low to high persistence, identified as P1, P2, or P3. Bioaccumulation is important because substances that bioaccumulate in aquatic and/or terrestrial species pose the potential for elevated exposures to humans and other organisms via the food chain. Bioaccumulation scores are, going from low to high bioaccumulation, identified as B1, B2, or B3. The toxicity score (T) is usually only used when the P and B scores are both a value of 2 or 3; in which case the chronic toxicity (to environmental organisms or human health) is assigned a value as described in the 1999 policy.

The environmental fate assessment utilized a similar tiered approach as the environmental hazard and human health teams to evaluate environmental persistence and bioaccumulation potential. However, a conservative-based weight of evidence approach was also utilized for persistence.

NCD acknowledges that biodegradation is not the only fate endpoint used to evaluate persistence. Likewise, experimentally-derived data were not always available (Tiers 1, 2 and 3) on all of the fate endpoints, and, as a result, Tier 4 data (predicted data for the constituents) were also used to justify the ratings. The added weight of evidence approach was also utilized to ensure that the experimentally-derived constituent biodegradation data (Tier 3) were weighted higher than the experimentally-derived data on a sufficiently similar fuel mixture (Tier 2) if one or more of the individual constituents (Tier 3) did not show ready biodegradation. In other words, if the experimentally-derived constituent data (Tier 3) were more conservative than the experimentally-derived data on a sufficiently similar fuel mixture (Tier 2), those constituent data were weighted higher than Tier 2 data. Additionally, NCD relied on experimental and predicted bioaccumulation and bioconcentration data on the dominant constituents (Tiers 3 and 4) in the assessment of bioaccumulation potential because Tiers 1 and 2 contained no data to assess bioaccumulation potential.

NCD estimated that the NCSs could have limited persistence or be very persistent (“P1-P3”) based on the aerobic and anaerobic biodegradation half-lives of the constituents (Tiers 3 and 4). NCD estimated that the NCSs could have limited persistence (“P1”) or limited persistence to being very persistent (“P1-P3”) and low potential for bioaccumulation (“B1”), low to moderate potential for bioaccumulation (“B1-B2”), or low to high potential for bioaccumulation (“B1-B3”) depending on the data for the constituents. P-21-0162 and P-21-0163 received a P1 and B1, and P-21-0146, P-21-0160, and P-21-0161

[redacted]

received a P1-P3 and B1. P-21-0147, P-21-0148 and P-21-0150 received a P1-P3 and B1-B2. The remaining cases received a P1-P3 and B1-B3. Repeated exposures may cause food-chain effects via accumulation in exposed organisms.

Table 4. Environmental Fate Predictions for P-21-0144, P-21-0145, P-21-0146, P-21-0147

Property	P-21-0144	P-21-0145	P-21-0146	P-21-0147
POTW removal (%)	90 to 99% via stripping, possible sorption and possible biodegradation	90 to 99% via stripping, sorption and possible biodegradation	90 to 99% via stripping, possible sorption and possible biodegradation	90 to 99% via stripping, possible sorption and possible biodegradation
Volatilization/Stripping	Moderate to extensive based on high estimated vapor pressure and Henry's Law constants for constituents	Extensive based on high estimated vapor pressure and Henry's Law constants for constituents	Extensive based on high estimated vapor pressure and Henry's Law constants for constituents	Moderate to extensive based on high estimated vapor pressure and Henry's Law constants for constituents
Aerobic and anaerobic biodegradation half-lives	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months to greater than 6 months based on half-lives for constituents
Sorption to soils/sediments	Low to very strong based on estimated K_{OC}s and K_{OW}s for constituents	Moderate to very strong based on estimated K_{OC}s and K_{OW}s for constituents	Low to very strong based on estimated K_{OC}s and K_{OW}s for constituents	Low to very strong based on estimated K_{OC}s and K_{OW}s for constituents
Migration to groundwater	Negligible to rapid based on low to very strong sorption to soil and sediment	Negligible to moderate based on moderate to very strong sorption to soil and sediment	Negligible to rapid based on low to very strong sorption to soil and sediment	Negligible to rapid based on low to very strong sorption to soil and sediment
Atmospheric oxidation half-life	Moderate to rapid based on hydroxyl radical half-lives for constituents	Moderate to rapid based on hydroxyl radical half-lives for constituents	Slow to moderate based on hydroxyl radical half-lives for constituents	Slow to rapid based on hydroxyl radical half-lives for constituents
Bioconcentration factor	56 estimated by linear regression from the log Kow for [redacted]	40 estimated by linear regression from the log Kow for [redacted]	29 estimated by linear regression from the log Kow for [redacted]	5 measured for [redacted]
Bioaccumulation factor	7,892 estimated by the Arnot-Gobas method (2003) for 2-[redacted]	33,260 estimated by the Arnot-Gobas method (2003) for 2,6-[redacted]	820 estimated by the Arnot-Gobas method (2003) for [redacted]	1,404 estimated by the Arnot-Gobas method (2003) for [redacted]
PBT Potential	P1-P3 limited persistence to very	P1-P3 limited persistence to very	P1-P3 limited persistence to very	P1-P3 limited persistence to very persistent based

[redacted]

Table 4. Environmental Fate Predictions for P-21-0144, P-21-0145, P-21-0146, P-21-0147				
	persistent based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B3: low to high bioaccumulation potential based on BCFBAF model result < 1000 to > 5000.	persistent based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B3: low to high bioaccumulation potential based on BCFBAF model result < 1000 to > 5000.	persistent based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1: low bioaccumulation potential based on BCFBAF model result < 1000.	on the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B2: low to moderate bioaccumulation potential based on BCFBAF model result < 1000 and > 1000 to < 5000.

Table 5. Environmental Fate Predictions for P-21-0148, P-21-0149, P-21-0150, P-21-0152				
Property	**P-21-0148**	**P-21-0149**	**P-21-0150**	**P-21-0152**
POTW removal (%)	90 to 99% via stripping, possible sorption and possible biodegradation	90 to 99% via stripping, possible sorption and possible biodegradation	90 to 99% via stripping, possible sorption and possible biodegradation	90 to 99% via stripping, sorption and possible biodegradation
Volatilization/ Stripping	Moderate to extensive based on moderate to high estimated vapor pressure and Henry's Law constants for constituents	Extensive based on high reported vapor pressure and Henry's Law constants for constituents	Moderate to extensive based on moderate to high estimated vapor pressure and Henry's Law constants for constituents	Low to extensive based on variable estimated vapor pressure and Henry's Law constants for constituents
Aerobic and anaerobic biodegradation half-lives	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months to greater than 6 months based on half-lives for constituents
Sorption to soils/sediments	Low to very strong based on estimated K_{OC}s and K_{OW}s for constituents	Low to very strong based on estimated K_{OC}s and K_{OW}s for constituents	Low to strong based on estimated K_{OC}s and K_{OW}s for constituents	Very strong based on estimated K_{OC}s and K_{OW}s for constituents
Migration to groundwater	Negligible to rapid based on low to very strong sorption to soil and sediments	Negligible to rapid based on low to very strong sorption to soil and sediment	Slow to rapid based on low to strong sorption to soil and sediment	Negligible based on very strong sorption to soil and sediment
Atmospheric oxidation half-life	Slow to rapid based on hydroxyl radical half-lives for constituents	Slow to rapid based on hydroxyl radical half-lives for constituents	Slow to moderate based on hydroxyl radical half-lives for constituents	Rapid based on hydroxyl radical half-lives for constituents
Bioconcentration factor	2,200 measured for [redacted]	5 measured for o-[redacted]	12 estimated by linear regression from the log Kow for [redacted]	3.2 estimated by linear regression from the log Kow for numerous constituents

[redacted]

Table 5. Environmental Fate Predictions for P-21-0148, P-21-0149, P-21-0150, P-21-0152				
Bioaccumulation factor	1,023 estimated by the Arnot-Gobas method (2003) for [redacted]	511,500 estimated by the Arnot-Gobas method (2003) for [redacted]	2,014 estimated by the Arnot-Gobas method (2003) for [redacted]	417,600 estimated by the Arnot-Gobas method (2003) for [redacted]
PBT Potential	P1-P3 limited persistence to very persistent based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B2: low to moderate bioaccumulation potential based on BCFBAF model result < 1000 and > 1000 to < 5000.	P1-P3 limited persistence to very persistent based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B3: low to high bioaccumulation potential based on BCFBAF model result < 1000 to > 5000.	P1-P3 limited persistence to very persistent based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B2: low to moderate bioaccumulation potential based on BCFBAF model result < 1000 and > 1000 to < 5000.	P1-P3 limited persistence to very persistent based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B3: low to high bioaccumulation potential based on BCFBAF model result < 1000 to > 5000.

Table 6. Environmental Fate Predictions for P-21-0153, P-21-0154, P-21-0155, P-21-0156, P-21-0157					
Property	**P-21-0153**	**P-21-0154**	**P-21-0155**	**P-21-0156**	**P-21-0157**
POTW removal (%)	90 to 99% via stripping, sorption and possible biodegradation	90 to 99% via sorption, possible stripping and possible biodegradation	90 to 99% via sorption, possible stripping and possible biodegradation	90 to 99% via stripping, sorption and possible biodegradation	90 to 99% via stripping, sorption and possible biodegradation
Volatilization/ Stripping	Moderate to extensive based on high estimated vapor pressure and Henry's Law constants for constituents	Low to extensive based on variable estimated vapor pressure and Henry's Law constants for constituents	Low to extensive based on variable estimated vapor pressure and Henry's Law constants for constituents	Moderate to extensive based on variable estimated vapor pressure and Henry's Law constants for constituents	Moderate to extensive based on variable estimated vapor pressure and Henry's Law constants for constituents
Aerobic and anaerobic biodegradation half-lives	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months to greater than 6 months based on half-lives for constituents
Sorption to soils/sediments	Strong to very strong based on estimated K_{OC}s and K_{OW}s for constituents	Strong to very strong based on estimated K_{OC}s and K_{OW}s for constituents	Moderate to very strong based on estimated K_{OC}s and K_{OW}s for constituents	Moderate to very strong based on estimated K_{OC}s and K_{OW}s for constituents	Strong to very strong based on estimated K_{OC}s and K_{OW}s for constituents
Migration to groundwater	Negligible to slow based on strong to	Negligible to slow based on strong to	Negligible to moderate based on	Negligible to moderate based	Negligible to slow based on strong to

Table 6. Environmental Fate Predictions for P-21-0153, P-21-0154, P-21-0155, P-21-0156, P-21-0157

	very strong sorption to soil and sediments	very strong sorption to soil and sediment	moderate to very strong sorption to soil and sediment	on moderate to very strong sorption to soil and sediment	very strong sorption to soil and sediment
Atmospheric oxidation half-life	Rapid based on hydroxyl radical half-lives for constituents	Rapid based on hydroxyl radical half-lives for constituents	Moderate to rapid based on hydroxyl radical half-lives for constituents	Moderate to rapid based on hydroxyl radical half-lives for constituents	Slow to rapid based on hydroxyl radical half-lives for constituents
Bioconcentration factor	3.2 estimated by linear regression from the log Kow for numerous constituents	3.2 estimated by linear regression from the log Kow for [redacted] and reported data for anthracene	41 measured for [redacted]	23 measured for [redacted]	5 measured from [redacted]
Bioaccumulation factor	10,990, 000 estimated by the Arnot-Gobas method (2003) for [redacted]	808,300 estimated by the Arnot-Gobas method (2003) for [redacted]	808,300 estimated by the Arnot-Gobas method (2003) for [redacted]	808,300 estimated by the Arnot-Gobas method (2003) for [redacted]	1,685,000 estimated by the Arnot-Gobas method (2003) for [redacted]
PBT Potential	P1-P3 limited persistence to very persistent based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B3: low to high bioaccumulation potential based on BCFBAF model result < 1000 to > 5000.	P1-P3 limited persistence to very persistent based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B3: low to high bioaccumulation potential based on BCFBAF model result < 1000 to > 5000.	P1-P3 limited persistence to very persistent based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B3: low to high bioaccumulation potential based on BCFBAF model result < 1000 to > 5000.	P1-P3 limited persistence to very persistent based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B3: low to high bioaccumulation potential based on BCFBAF model result < 1000 to > 5000.	P1-P3 limited persistence to very persistent based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B3: low to high bioaccumulation potential based on BCFBAF model result < 1000 to > 5000.

Table 7. Environmental Fate Predictions for P-21-0158, P-21-0160, P-21-0161, P-21-0162, P-21-0163

Property	P-21-0158	P-21-0160	P-21-0161	P-21-0162	P-21-0163
POTW removal (%)	90 to 99% via stripping, sorption and possible biodegradation	90 to 99% via stripping, possible sorption and possible biodegradation	90 to 99% via stripping, possible sorption and possible biodegradation	90 to 99% via stripping, possible sorption and biodegradation	90 to 99% via stripping, possible sorption and biodegradation

[redacted]

Table 7. Environmental Fate Predictions for P-21-0158, P-21-0160, P-21-0161, P-21-0162, P-21-0163

Volatilization/Stripping	Moderate to extensive based on moderate to high estimated vapor pressure and Henry's Law constants for constituents	Moderate to extensive based on high estimated vapor pressure and Henry's Law constants for constituents	Moderate to extensive based on high estimated vapor pressure and Henry's Law constants for constituents	Extensive based on high estimated vapor pressure and Henry's Law constants for constituents	Extensive based on high estimated vapor pressure and Henry's Law constants for constituents
Aerobic and anaerobic biodegradation half-lives	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months to greater than 6 months based on half-lives for constituents	Less than 2 months based on half-lives for constituents	Less than 2 months based on half-lives for constituents
Sorption to soils/sediments	Moderate to very strong based on estimated K_{OC}s and K_{ow}s for constituents	Low to moderate based on estimated K_{OC}s and K_{ow}s for constituents	Low to moderate based on estimated K_{OC}s and K_{ow}s for constituents	Low to strong based on estimated K_{OC}s and K_{ow}s for constituents	Low to moderate based on estimated K_{OC}s and K_{ow}s for constituents
Migration to groundwater	Negligible to moderate based on moderate to very strong sorption to soil and sediments	Moderate to rapid based on low to moderate sorption to soil and sediments	Moderate to rapid based on low to moderate sorption to soil and sediment	Negligible due to biodegradation	Negligible due to biodegradation
Atmospheric oxidation half-life	Moderate to rapid based on hydroxyl radical half-lives for constituents	Slow to rapid based on hydroxyl radical half-lives for constituents	Slow to rapid based on hydroxyl radical half-lives for constituents	Slow to moderate based on hydroxyl radical half-lives for constituents	Slow based on hydroxyl radical half-lives for constituents
Bioconcentration factor	40 estimated by linear regression from the log Kow for [redacted]	7 estimated by linear regression from the log Kow for [redacted]	7 estimated by linear regression from the log Kow for [redacted]	29 estimated by linear regression from the log Kow for [redacted]	17 estimated by linear regression from the log Kow for [redacted]
Bioaccumulation factor	4,709,000 estimated by the Arnot-Gobas method (2003) for [redacted]	61 estimated by the Arnot-Gobas method (2003) for [redacted]	47 estimated by the Arnot-Gobas method (2003) for [redacted]	310 estimated by the Arnot-Gobas method (2003) for [redacted]	148 estimated by the Arnot-Gobas method (2003) for [redacted]
PBT Potential	P1-P3 limited persistence to very persistent based on	P1-P3 limited persistence to very persistent	P1-P3 limited persistence to very persistent based on	P1 limited persistence based on the aerobic	P1 limited persistence based on the aerobic and

[redacted]

Table 7. Environmental Fate Predictions for P-21-0158, P-21-0160, P-21-0161, P-21-0162, P-21-0163					
	the aerobic and anaerobic biodegradation half-lives of the constituents. B1-B3: low to high bioaccumulation potential based on BCFBAF model result < 1000 to > 5000.	based on the aerobic and anaerobic biodegradation half-lives of the constituents. B1: low bioaccumulation potential based on BCFBAF model result < 1000.	the aerobic and anaerobic biodegradation half-lives of the constituents. B1: low bioaccumulation potential based on BCFBAF model result < 1000.	biodegradation half-lives of the constituents. B1: low bioaccumulation potential based on BCFBAF model result < 1000.	anaerobic biodegradation half-lives of the constituents. B1: low bioaccumulation potential based on BCFBAF model result < 1000.

[redacted]

4 ENVIRONMENTAL HAZARD AND CONCENTRATION-RESPONSE ASSESSMENT

The waste-plastic derived fuel streams assessed in this report (P-21-0144, P-21-0145, P-21-0146, P-21-0147, P-21-0148, P-21-0149, P-21-0150, P-21-0152, P-21-0153, P-21-0154, P-21-0155, P-21-0156, P-21-0157, P-21-0158, P-21-0160, P-21-0161, P-21-0162, and P-21-0163) are chemical mixtures classified as UVCBs. Their environmental hazard assessment requires informed and flexible approaches to accommodate the limited data availability and inherent complexity (*e.g.,* interactive effects of the constituents) of these types of chemicals. Therefore, the environmental hazard assessments of the NCSs applied a four-tiered, hierarchical approach as described in Appendix A. Briefly, with a lack of data on the actual NCSs (Tier 1), in order to assign hazard and determine the acute and chronic concentrations of concern (COCs), this hazard approach relied on the availability of:

- experimentally-derived environmental hazard data on analogous fuel streams (Tier 2, Appendix B),
- predicted environmental hazard data from the hydrocarbon constituents and toxic units (Tier 3), or
- predicted environmental hazard data on the most toxic hydrocarbon constituents (Tier 4).

Environmental Hazard Assessment for the Waste-Plastic Derived Fuel Streams

Nine of the NCSs, P-21-0145, P-21-0146, P-21-0147, P-21-0148, P-21-0149, P-21-0150, P-21-0155, P-21-0156, and P-21-0158, were evaluated using acceptable hazard data from four analogous fuel streams (Tier 2) with CASRNs 64741-66-8[3], 64741-55-5[2], 64741-59-9[4], and 64741-77-1[3]. These fuel streams were considered analogous based on the sufficient similarity with the NCSs, as outlined in Appendix A. The acute and chronic ecotoxicity endpoints for fish, aquatic invertebrates, and algae for each of the four fuel stream analogues are listed in Table 8, with studies summarized in Appendix B.

Table 8. Summary of Ecotoxicity Endpoint Data (ppm) for Analogous Fuel Streams (Tier 2)

Endpoint	Source	CASRN: 64741-66-8	CASRN: 64741-55-5	CASRN: 64741-59-9	CASRN: 64741-77-1
Fish 96-h LC_{50}	Experimentally-derived	**0.305**	4.1	>0.21	>0.54
Aquatic Invertebrate 48-h EC_{50}	Experimentally-derived	0.556	**1.4**	0.45	1
Algae 96-h EC_{50}	Experimentally-derived	0.741	4.6	**0.22**	**0.51**
Fish ChV	ACR 10	**0.031**	0.41	**0.031***	**0.031***
Aquatic Invertebrate ChV	Experimentally-derived	0.052	**0.17**	0.053	>0.13****
Algae ChV	ACR 4	0.185	1.15	0.055	0.128

Bold indicates the endpoints used for acute and chronic COC determination

[3]U.S. Environmental Protection Agency Hazard Characterization Document: Screening-Level Hazard Characterization of Gasoline Blending Streams Category (December, 2011).

[4]The American Petroleum Institute (API) Petroleum HPV Testing Group: Gas Oils Category Analysis Document and Hazard Characterization (Consortium #1100997) submitted to the EPA (October, 2012).

[redacted]

ChV= chronic value as defined by the geometric mean of the lowest observed effect concentration (LOEC) and the no observed effect concentration (NOEC), unless an ACR was used
ACR= acute to chronic ratio
*ACRs are not applied to NOEC values from acute tests; most toxic endpoint of the 81 petroleum refinery streams in the gasoline blending streams category[1]
**Measured 21-day LOEC is >0.13 ppm

When Tier 2 information was not available, NCSs were assessed using the predicted toxicity of the individual constituents and the Toxic Unit (TU) approach. Fuel-stream mixtures are comprised of hydrocarbons, which are classified as neutral organic compounds that assert toxicity via non-polar narcosis. Because hydrocarbons share this common, additive toxic mode of action, the toxicity of fuel-stream mixtures is assumed to result from the additive contribution of each constituent (Capuzzo 1987, Di Toro and McGrath 2000, Barata et al. 2005, McGrath et al. 2005, Redman et al. 2012)[5]. The TU approach is a hazard index that characterizes mixture toxicity by combining the toxic contributions of the individual constituents (described in detail in Appendix D).

The application of TUs to the nine remaining fuel stream NCSs required detailed information describing the constituents of each submission. Four of the nine NCSs assessed with Tier 3 test data (P-21-0160, P-21-0161, P-21-0162, and P-21-0163) were submitted with ≥ 93% of the fuel stream hydrocarbon constituents identified, according to the Chemistry report (10-18-21). The toxicities of the identified constituents were characterized using modeled data from the Ecological Structure Activity Relationships (ECOSAR) Predictive Model (https://www.epa.gov/tsca- screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model); specifically the QSAR for neutral organics. The full list of acute and chronic ecotoxicity endpoints for fish, aquatic invertebrates, and algae (for each constituent) can be found in Table E-1 (Appendix E). The TUs based on 1 ppm total fuel-stream concentration were used to estimate acute and chronic ecotoxicity endpoints for each NCS using the equations in Appendix D. Table 9 contains the summarized information for the most sensitive organism[6] used in the hazard assessment of these four NCSs (P-21-0160, P-21-0161, P-21-0162, and P-21-0163), while Table E-3 (Appendix E) provides the ecotoxicity endpoints for all taxa of interest.

Fuel-stream constituents were not identified to the chemical level for the remaining five NCSs (P-21-0144, P-21-0152, P-21-0153, P-21-0154, and P-21-0157); therefore, TUs were calculated using representative constituents for each class that were within the range of the physical properties for each NCS. The process for selecting these representative constituents is summarized in more detail in Appendix D. Briefly, the log K_{OW} limits used to determine representative constituents were consistent with observed effects of neutral organic chemicals in additive mixtures; constituents with log $K_{OW} < 7.0$ were used for acute effects, while chronic effects used constituents with log $K_{OW} < 8.0$. The toxicities of the identified constituents within these limits, and within the properties of the specific fuel-stream (carbon range, PIONA class, etc.), were characterized using modeled data from ECOSAR. The most toxic constituents were selected as representatives for each PIONA class (or subclass) fraction that was indicated in the Chemistry report. Although this approach provided an inherently conservative

[5] Full citations for references are after Appendix D.

[6] Most sensitive organism is determined by the lowest COCs following downstream calculation and application of assessment factors for the neutral organics chemical class.

[redacted]

estimate of mixture toxicity, this worst-case scenario approach is necessary to avoid underestimating mixture effects when the identities of the constituents are unknown.

The acute and chronic ecotoxicity endpoints for fish, aquatic invertebrates, and algae for the representative constituents used in the hazard assessment of these five NCSs (P-21-0144, P-21-0152, P-21-0153, P-21-0153, and P-21-0154) are listed in Table E-2 (Appendix E). As before, the TUs were calculated for each fuel-stream NCS and used to estimate the acute and chronic ecotoxicity endpoints for all taxa of interest (Table E-3, Appendix E). Table 10 contains the summarized information for the most sensitive organism used in the hazard assessment of these five NCSs.

[redacted]

Table 9. Summarized Environmental Hazard Assessments for Fuel-Stream NCSs that Used Detailed Chemical Composition and the Toxic Unit Approach

NCS	Class[A]-stream fraction	Chemical name CASRN	Chemical fraction	Acute Toxicity			Chronic Toxicity		
				Endpoint[B] (ppm)	TUs[C] at 1 ppm	TU Endpoint[D] (ppm)	Endpoint[B] (ppm)	TUs[C] at 1 ppm	TU Endpoint[D] (ppm)
P-21-0160	[redacted]			14.82	0.00675		1.56	0.0640	
				17.13	0.02218		1.77	0.2142	
				8.06	0.00744		0.95	0.0634	
				18.73	0.02136		1.91	0.2097	
				10.36	0.00193		1.17	0.0170	
					0.05966	**16.76**	-	0.5683	**1.76**
P-21-0161				14.82	0.01215		1.56	0.1151	
				17.13	0.03794		1.77	0.3665	
				8.06	0.00744		0.95	0.0634	
				18.73	0.00214		1.91	0.0210	
					0.05966	**16.76**		0.5660	**1.77**
P-21-0162				6.97	0.0330		0.83	0.2757	
				14.82	0.0121		1.56	0.1151	
				3.65	0.0795		0.49	0.5965	
				8.06	0.0335		0.95	0.2852	
					0.1581	**6.32**		1.2725	**0.79**

[**P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163**]

[redacted]

NCS	Class[A]-stream fraction	Chemical name CASRN	Chemical fraction	Acute Toxicity			Chronic Toxicity		
				Endpoint[B] (ppm)	TUs[C] at 1 ppm	TU Endpoint[D] (ppm)	Endpoint[B] (ppm)	TUs[C] at 1 ppm	TU Endpoint[D] (ppm)
P-21-0163	[redacted]			14.817746	0.03644		1.56	0.3454	
				6.971164	0.00717		0.83	0.0599	
				17.133465	0.01634		1.77	0.1579	
				8.060612	0.01117		0.95	0.0951	
					0.07112	**14.06**		0.6583	**1.52**

[A]Class refers to the PIONA class (P= paraffin, I= isoparaffin, O= olefins, N= naphthenic, A= aromatic);
[B]The endpoint for fish, aquatic invertebrate, or algae that resulted in the lowest COC following application of assessment factors;
[C] Toxic Units = (Chemical fraction * 1 ppm)/ endpoint;
[D] The predicted endpoint using the respective TUs (= 1/ total TU @ 1ppm)
BOLD indicates the predicted total fuel stream endpoint used for COC determination

[redacted]

Table 10. Summarized Environmental Hazard Assessments for the Fuel-Stream NCSs that Used the Toxic Unit Approach with Representative Constituents for Each Hydrocarbon Class or Subclass

NCS	Class[A] stream fraction	Subclass[B] stream fraction	Acute				Chronic			
			Chemical[C] CASRN/SMILES	Endpoint[D] (ppm)	TUs[E] at 1 ppm	TU Endpoint[F] (ppm)	Chemical CASRN/SMILES	Endpoint[D] (ppm)	TUs[E] at 1 ppm	TU Endpoint[F] (ppm)
P-21-0144	[redacted]	[redacted]	[redacted]	0.26	0.156		[redacted]	0.001	28.57	
				0.29	0.612			0.004	45.56	
				0.69	0.087			0.123	0.49	
				0.36	0.333			0.002	59.73	
				0.56	1.070			0.101	5.97	
				-	2.257	**0.443**		-	140.32	**0.007**
P-21-0152				No toxicity predicted; minimum log K_{OW} > 7				No toxicity predicted; minimum log K_{OW} > 8		
				0.007	73.24			0.0002	2095.91	
				0.015	27.31			0.0027	147.12	
					100.55	**0.010**			2243.02	**0.0004**
P-21-0153				No toxicity predicted; minimum log K_{OW} > 7				No toxicity predicted; minimum log K_{OW} > 8		
				No toxicity contribution; minimum log K_{OW} > 7				0.0002	1884.06	
				0.020	7.50			0.0004	384.62	

[redacted]

NCS	Class[A] stream fraction	Subclass[B] stream fraction	Acute				Chronic			
			Chemical[C] CASRN/SMILES	Endpoint[D] (ppm)	TUs[E] at 1 ppm	TU Endpoint[F] (ppm)	Chemical CASRN/SMILES	Endpoint[D] (ppm)	TUs[E] at 1 ppm	TU Endpoint[F] (ppm)
	[redacted]	[redacted]	[redacted]				[redacted]			
				0.073	0.41			0.0004	81.43	
				0.014	2.14			0.0002	150.0	
					10.05	**0.099**			2500.1	**0.0004**
P-21-0154				No toxicity predicted; minimum log K_{OW} > 7				No toxicity predicted; minimum log K_{OW} > 8		
				0.015	15.11			0.0002	1381.64	
				0.092	1.30			0.0002	624.38	
				0.155	0.52			0.0004	220.69	
				0.026	1.51			0.0004	108.57	
				0.083	2.40			0.0002	1143.88	
				0.308	0.32			0.0003	357.53	
				0.809	0.04			0.0002	125.75	

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

NCS	Class[A] stream fraction	Subclass[B] stream fraction	Acute				Chronic			
			Chemical[C] CASRN/SMILES	Endpoint[D] (ppm)	TUs[E] at 1 ppm	TU Endpoint[F] (ppm)	Chemical CASRN/SMILES	Endpoint[D] (ppm)	TUs[E] at 1 ppm	TU Endpoint[F] (ppm)
P-21-0157	[redacted]	[redacted]	[redacted]	0.289	0.07		[redacted]	0.0069	2.90	
					21.27	**0.047**			3965.35	**0.0003**
				No toxicity predicted; minimum log K_{OW} > 7				0.0002	986.66	
				0.064	3.13			0.0008	241.42	
				0.406	0.49			0.0004	511.24	
				0.156	0.96			0.0004	413.79	
				0.315	0.48			0.0002	861.93	
				0.308	0.06			0.0003	62.18	
					5.12	**0.195**			3015.03	**0.0003**

[A]Class refers to the PIONA class (P= paraffin, I= isoparaffin, O= olefins, N= naphthenic, A= aromatic);
[B]The highest resolution constituent information listed in the chemistry report;
[C]The representative chemical with the highest toxicity in each subclass;
[D]The endpoint for fish, aquatic invertebrate, or algae that resulted in the lowest COC following application of assessment factors;
[E]Toxic Units = (Chemical fraction * 1 ppm)/ endpoint;
[F]The predicted endpoint using the respective TUs (= 1/ total TU @ 1ppm);
[redacted] was used to represent the aromatics, because it was the most toxic listed, and only [redacted]% of aromatics were accounted for (none listed above [redacted]%)
BOLD indicates the predicted total fuel stream endpoint used for COC determination

[redacted]

The estimated ecotoxicity endpoints for the 18 fuel-stream mixtures included in this report are summarized in Table E-3 (Appendix E). Nine NCSs used Tier 2 analogous fuel streams (Table 11), and nine NCSs used Tier 3 constituent-based information and toxic units (Table 12) to assess acute and chronic environmental hazard. The lowest acute and chronic toxicity endpoints for each NCS were used to determine the environmental hazard and calculate the acute and chronic COCs. The lowest estimated acute toxicity endpoints for each NCS were all between 0.005 and 16.76 ppm, while chronic toxicity endpoints were all between 0.0003 and 1.77 ppm. As per established EPA/OPPT methods, the application of assessment factors of 4 (algae) or 5 (fish and aquatic invertebrates) to the acute toxicity values results in acute COCs between 0.002 ppm (2 ppb) and 3.352 ppm (3352 ppb). As per established EPA/OPPT methods, application of an assessment factor of 10 to chronic toxicity values (*i.e.,* ChV) results in chronic COCs between 0.00003 ppm (0.03 ppb) and 0.177 ppm (177 ppb). The acute and chronic aquatic toxicity endpoints indicate that the NCSs are expected to range from moderate to high environmental hazard.

Table 11. Hazard Rating and Associated COCs for NCSs Assessed with Tier 2 Analogous Fuel Streams

NCS	Analogue[A] CASRN(s)	Acute				Chronic			
		End-point[B] (ppm)	Hazard Rating[C]	AF	COC (ppb)	End-point[B] (ppm)	Hazard Rating[C]	AF	COC (ppb)
P-21-0147 P-21-0148 P-21-0150	64741-55-5	1.4	2	5	280	0.17	2	10	17
P-21-0145 P-21-0146 P-21-0149	64741-66-8	0.305	3	5	61	0.031	3	10	3
P-21-0158	64741-77-1 & 64741-66-8[D]	0.510	3	4	128	0.031	3	10	3
P-21-0155 P-21-0156	64741-59-9& 64741-66-8[D]	0.220	3	4	55	0.031	3	10	3

[A]Refers to the fuel stream analogue (Tier 2) used for assessment

[B] The endpoint for fish, aquatic invertebrate, or algae that resulted in the lowest COC following application of assessment factors;

[C]Hazard Rating: 1 = Low, 2 = Moderate, 3 = High

[D]Most toxic endpoint (fish chronic value) of the 81 petroleum refinery streams in the gasoline blending streams category[7];

AF= Assessment Factor (acute fish and aquatic invertebrate =5, acute algae = 4, all chronic = 10);

COC= Concentration of Concern

[7]U.S. Environmental Protection Agency Hazard Characterization Document: Screening-Level Hazard Characterization of Gasoline Blending Streams Category (December, 2011).

[redacted]

Table 12. Hazard Rating and Associated COCs for NCSs Assessed with Tier 3 Composition Data and Toxic Units

NCS	Stream % used for TUs[A]	Acute				Chronic			
		End-point[B] (ppm)	Hazard Rating[C]	AF	COC (ppb)	End-point[B] (ppm)	Hazard Rating[C]	AF	COC (ppb)
P-21-0144	100%	0.443	3	5	89	0.007	3	10	0.7
P-21-0152	94%	0.010	3	5	2	0.0004	3	10	0.04
P-21-0153	97%	0.099	3	5	20	0.0004	3	10	0.04
P-21-0154	97%	0.047	3	5	9	0.0003	3	10	0.03
P-21-0157	95%	0.195	3	5	39	0.0003	3	10	0.03
P-21-0160	96%	16.76	2	5	3352	1.76	2	10	176
P-21-0161	93%	16.76	2	5	3352	1.77	2	10	177
P-21-0162	97%	6.324	2	5	1265	0.79	2	10	79
P-21-0163	96%	14.06	2	5	2812	1.52	2	10	152

[A]The percent of the fuel stream NCS that was identified and used for toxic unit calculation
[B]The endpoint for fish, aquatic invertebrate, or algae that resulted in the lowest COC following application of assessment factors;
[C]Hazard Rating: 1 = Low, 2 = Moderate, 3 = High
AF= Assessment Factor (acute fish and aquatic invertebrate =5, acute algae = 4, all chronic = 10)
COC= Concentration of Concern

5 HUMAN HEALTH HAZARD AND DOSE-RESPONSE ASSESSMENT

5.1 Background to Human Health Hazard Assessment

US EPA considered available information on absorption, structural alerts and chemical categories, SDS data, and exposure routes to inform the human health hazard assessment of the NCSs.

5.1.1 Absorption

Absorption of the NCSs through the skin, gastrointestinal tract, and lungs was estimated based on physical/chemical properties (form, molecular weight, water solubility, log P partition coefficient, and vapor pressure). Table 13 shows the qualitative absorption estimates.

[redacted]

Table 13. Qualitative Estimates of Absorption of New Chemical Substances based on Physical-Chemical Properties			
Case	Skin[a]	Gastrointestinal Tract	Lungs
P-21-0144	Good	Good	Poor
P-21-0145	Moderate	Moderate	Poor
P-21-0146	Moderate	Moderate	Poor
P-21-0147	Good	Good	Poor
P-21-0148	Moderate	Moderate	Poor
P-21-0149	Moderate	Moderate	Poor
P-21-0150	Moderate	Moderate	Poor
P-21-0152	Moderate	Nil	Nil
P-21-0153	Moderate	Nil	Nil
P-21-0154	Moderate	Nil	Nil
P-21-0155	Moderate	Moderate	Poor
P-21-0156	Moderate	Moderate	Poor
P-21-0157	Moderate	Moderate	Poor
P-21-0158	Moderate	Moderate	Poor
P-21-0160	Nil	Nil	Poor
P-21-0161	Nil	Nil	Poor
P-21-0162	Nil	Nil	Poor
P-21-0163	Nil	Nil	Poor
[a]Skin irritation is expected to increase dermal uptake for all cases with the exception of P-21-0160-0163, which are gases when neat.			

5.1.2 Structural Alerts

Hydrocarbons

5.1.3 Human Health Category (From US EPA 2010 document)

Not applicable.

5.1.4 OECD QSAR Toolbox

The NCSs were not analyzed using the OECD QSAR Toolbox because they are complex mixtures and outside the domain of applicability of the software.

5.1.5 SDS Data

The submitted SDSs are for formulations containing the new chemical substance at [redacted]% weight of the mixture.

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

5.1.6 Other Information

None

5.1.7 Exposure Routes of Interest

Exposure to the NCSs is expected to occur through all routes (inhalation, dermal, and ingestion) based on physical/chemical properties, environmental fate, and engineering assessments.

5.2 Human Health Hazard Information

Hazards of the NCSs were identified based on Tier 2 analogous mixtures and Tier 3 representative constituents (see Appendix A for description of Tiers) and based on physical/chemical properties and structure. For the NCSs, EPA identified the hazards shown in Table 14. Refer to Appendix F for the toxicological information supporting the evaluation of human health hazards.

[redacted]

Table 14. Summary of Hazard Concerns for Waste Plastics (P-21-0144-0150, P-21-0152-0153)										
Hazard Category		**P-21-0144**	**P-21-0145**	**P-21-0146**	**P-21-0147**	**P-21-0148**	**P-21-0149**	**P-21-0150**	**P-21-0152**	**P-21-0153**
Irritation	**Eye**	x	x	x	x	x	x	x		x
	Skin	x	x	x	x	x	x	x	x	x
	Respiratory	x	x	x	x	x	x	x	x	x
Acute Toxicity		x	x	x	x	x	x			
Developmental Toxicity		x	x	x	x	x	x	x	x	x
Reproductive Toxicity		x			x	x		x	x	x
Systemic Toxicity	**Neurotoxicity**	x	x	x	x	x	x	x	x	
	Body weight	x	x	x	x	x	x	x	x	x
	Liver	x	x	x	x	x		x	x	x
	Kidney	x	x	x	x	x	x	x		x
	Blood	x		x	x	x	x	x	x	x
	Spleen	x	x	x				x		x
	Other	lung		lung	adrenal, thyroid			adrenal, thyroid	lung, thymus,	heart, pituitary, thymus, thyroid, para-thyroid
Portal of Entry	**Oral**	x	x	x				x		
	Inhalation			x	x			x		
Aspiration Hazard		x	x	x	x	x	x	x	x	x
Genetic Toxicity		x		x	x	x		x	x	x
Carcinogenicity		x		x	x	x		x	x	x

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table 14 (Cont'd). Summary of Hazard Concerns for Waste Plastics (P-21-0154-0158, P-21-0160-0163)										
Hazard Category		**P-21-0154**	**P-21-0155**	**P-21-0156**	**P-21-0157**	**P-21-0158**	**P-21-0160**	**P-21-0161**	**P-21-0162**	**P-21-0163**
Irritation	**Eye**		x	x		x	x	x	x	x
	Skin	x	x	x	x	x	x	x		
	Respiratory	x	x	x	x	x	x	x	x	x
Acute Toxicity			x	x						
Developmental Toxicity		x	x	x	x				x	x
Reproductive Toxicity		x	x	x		x				
Systemic Toxicity	**Neurotoxicity**	x	x	x	x	x			x	x
	Body weight	x	x	x	x	x	x	x	x	x
	Liver	x	x	x	x	x			x	x
	Kidney	x	x	x	x	x	x	x	x	x
	Blood	x	x	x	x	x	x	x	x	x
	Spleen		x	x		x				
	Other	lung, thymus	adrenal, lung, thymus	adrenal, lung, thymus	lung, thymus	adrenal, lung				
Portal of Entry	**Oral**		x	x		x				
	Inhalation	x	x	x	x	x	x	x	x	x
Aspiration Hazard		x	x	x	x	x	x	x	x	x
Genetic Toxicity		x	x	x	x	x				
Carcinogenicity		x	x	x	x	x	x	x	x	x

[redacted]

5.3 Human Health Dose-Response Information: Selected Points of Departure (POD) and Basis

No human health hazard data were submitted for any of the 18 NCSs(Tier 1). NCD estimated the human health hazard of the NCSs based on estimated physical/chemical properties, by comparing it to compositionally analogous mixtures (Tier 2) for which there are information on human health hazard, using available human hazard information on representative constituents (Tier 3) of the new chemical substance, and other structural information.

The only composition information provided for each of the new chemical substance mixtures was the carbon range and the identification of a petroleum equivalent analogue for which carbon range and PIONA composition were available. Based on the carbon ranges of the NCSs and their petroleum equivalents, the PIONA composition of the petroleum equivalent, and available information on typical constituents of the petroleum equivalent (see Table 2), representative constituents of the NCS mixtures were identified for each PIONA class present in the mixture. Using a database of petroleum constituent PODs (see Appendix F), constituents of each PIONA class that are in the carbon range of the new chemical substance were identified. Hazards of the new chemical substance were identified based on information for the Tier 2 analogous mixtures and Tier 3 representative constituents.

For each exposure route, non-cancer risks of the new chemical substance were estimated using two approaches: 1) using the POD for the petroleum equivalent analogue (if available) or another analogous mixture; and 2) using the worst-case constituent[8] POD. These PODs provide complementary estimates of risk that are intended to address interaction effects of mixtures as well as data gaps in the endpoints evaluated in studies of mixtures. The combination of approaches is expected to be protective for hazards identified for the analogous mixtures and those identified for representative constituents of the new chemical substance. If no suitable analogous mixtures were identified for a specific exposure route, then the risks were based on the worst-case constituent. Similarly, for each exposure route, cancer risks were estimated using a POD for Tier 2 analogous mixture (if available) or the worst-case representative constituent (representative constituent with the highest cancer slope factor or inhalation unit risk).

Non-cancer:

Table 15 shows the Tier 2 analogous mixture(s) and Tier 3 worst-case constituents selected for each exposure route. Tables 16 through 18 show the non-cancer oral, inhalation, and dermal PODs for the analogous mixtures and worst-case constituents.

[8]The worst case constituent was the constituent with the lowest value obtained by dividing each POD (or its NOAEL-equivalent if the POD is a LOAEL) by the fraction represented by that PIONA class.

[redacted]

Table 15. Summary of Tier 2 Analogous Mixtures and Tier 3 Worst-Case Constituents Used for Non-cancer PODs							
Case number	**P-21-0144**	**P-21-0145**	**P-21-0146**	**P-21-0147**	**P-21-0148**	**P-21-0149**	**P-21-0150**
Petroleum equivalent	**64741-54-4**	**64741-65-7**	**68527-27-5**	**64742-48-9**	**64741-55-5**	**64741-66-8**	**64742-49-0**
Basis for Oral POD							
Tier 2 Analogous Mixture	64741-54-4*	64741-66-8	64741-66-8	64742-48-9*	64741-55-5*	64741-66-8*	None identified
Tier 3 Worst-Case Constituent	1,2,4-trimethyl benzene	n-nonane[a]	n-nonane	benzene	benzene	2-methyl pentane	n-nonane
Basis for Inhalation POD							
Tier 2 Analogous Mixture	64741-68-0	64741-66-8	64741-66-8	64741-41-9	64741-55-5*	64741-66-8*	64741-41-9
Tier 3 Worst-Case Constituent	dicyclopenta diene	dicyclopenta diene[a]	1-methyl naphthalene[b]	benzene	dicyclopenta diene	2-methyl pentane	benzene
Basis for Dermal POD							
Tier 2 Analogous Mixture	64741-68-0	64741-66-8	64741-66-8	64741-78-2	64741-55-5*	64741-66-8*	64741-78-2

*Indicates Tier 2 analogous mixture produced concurrently with the new chemical substance.

[a] The new chemical substance is expected to contain a nonzero percentage of one or more PIONA classes for which no representative constituent in the carbon range of the new chemical substance with a POD for the specified route was identified. Therefore, the worst-case for this route was selected using only the representative constituents identified for remaining classes and the corresponding percentages for these classes. In the absence of a representative constituent for one or more PIONA classes present in the new chemical substance, the selection of this representative constituent as the worst-case for this route is associated with additional uncertainty.

[redacted]

Table 15 (Cont'd). Summary of Tier 2 Analogous Mixtures and Tier 3 Worst-Case Constituents Used for Non-cancer PODs							
Case number	**P-21-0152**	**P-21-0153**	**P-21-0154**	**P-21-0155**	**P-21-0156**	**P-21-0157**	**P-21-0158**
Petroleum equivalent	**64741-62-4**	**64741-76-0**	**64742-59-2**	**64741-59-9**	**64742-38-7**	**64742-46-7**	**64742-47-8**
Basis for Oral POD							
Tier 2 Analogous Mixture	None identified	White mineral oil	None identified	None identified	None identified	None identified	64742-47-8*
Tier 3 Worst-Case Constituent	benzo[a] pyrene[a]	None identified	pyrene[a]	1,2,4-trimethyl benzene	1,2,4-trimethyl benzene	2-methyl naphthalene[a]	1,2,4-trimethyl benzene[a]
Basis for Inhalation POD							
Tier 2 Analogous Mixture	None identified	None identified	None identified	None identified	None identified	None identified	64742-47-8*
Tier 3 Worst-Case Constituent	benzo[a] pyrene[a]	None identified	benzo[a] pyrene[a]	1-methyl naphthalene	1-methyl naphthalene	1-methyl naphthalene[a]	1-methyl naphthalene[a]
Basis for Dermal POD							
Tier 2 Analogous Mixture	64741-62-4*	64742-05-8	64741-62-4	64741-59-9*	64741-59-9*	68334-30-5	None identified

*Indicates Tier 2 analogous mixture produced concurrently with the new chemical substance.

[a] The new chemical substance is expected to contain a nonzero percentage of one or more PIONA classes for which no representative constituent in the carbon range of the new chemical substance with a POD for the specified route was identified. Therefore, the worst-case for this route was selected using only the representative constituents identified for remaining classes and the corresponding percentages for these classes. In the absence of a representative constituent for one or more PIONA classes present in the new chemical substance, the selection of this representative constituent as the worst-case for this route is associated with additional uncertainty.

[redacted]

Table 15 (Cont'd). Summary of Tier 2 Analogous Mixtures and Tier 3 Worst-Case Constituents Used for Non-cancer PODs				
Case number	**P-21-0160**	**P-21-0161**	**P-21-0162**	**P-21-0163**
Petroleum equivalent	**68477-85-0**	**68783-64-2**	**68478-12-6**	**68478-32-0**
Basis for Oral POD				
Tier 2 Analogous Mixture	None identified	None identified	None identified	None identified
Tier 3 Worst-Case Constituent	1,3-pentadiene[a]	1,3-pentadiene[a]	2-methylpentane	2-methylpentane
Basis for Inhalation POD				
Tier 2 Analogous Mixture	isobutane/2-methylbutane mixture (50:50)	isobutane/2-methylbutane mixture (50:50)	Commercial hexane	Commercial hexane
Tier 3 Worst-Case Constituent	2-methyl propene[a]	2-methyl propene[a]	2-methyl pentane	2-methylpentane
Basis for Dermal POD				
Tier 2 Analogous Mixture	None identified	None identified	None identified	None identified

*Indicates Tier 2 analogous mixture produced concurrently with the new chemical substance.

[a] The new chemical substance is expected to contain a nonzero percentage of one or more PIONA classes for which no representative constituent in the carbon range of the new chemical substance with a POD for the specified route was identified. Therefore, the worst-case for this route was selected using only the representative constituents identified for remaining classes and the corresponding percentages for these classes. In the absence of a representative constituent for one or more PIONA classes present in the new chemical substance, the selection of this representative constituent as the worst-case for this route is associated with additional uncertainty.

[redacted]

Table 16. Non-Cancer Oral PODs for Analogous Mixtures (Tier 2) and Worst Case Constituents (Tier 3)							
Mixture or Constituent (CASRN)	**Tier**	**POD Type**	**POD (mg/kg/day)**	**POD Exposure Frequency (d/wk)**	**Adjusted POD (mg/kg/day)**	**Benchmark Margin of Exposure**	**Endpoint**
64741-54-4	2	LOAEL	500	5	357	1000	Decreased body weight
64741-55-5	2	NOAEL	500	5	357	100	Decreased body weight
64741-66-8	2	LOAEL	500	5	357	1000	Mortality
64742-47-8	2	LOAEL	500	5	357	1000	Blood, liver, and kidney
64742-48-9	2	NOAEL	5000	7	5000	100	None
White mineral oil (no CASRN)	2	NOAEL	870	7	870	10	None
1,2,4-Trimethylbenzene (95-63-6)	3	BMDL	3.5	7	3.5	100	Neurotoxicity
2-Methylpentane (107-83-5)	3	LOAEL	1000	7	1000	1000	Neurotoxicity
Benzene (71-43-2)	3	BMDL	1.2	7	1.2	10	Hematological/ immune
n-Nonane (111-84-2)	3	BMDL	3.13	7	3.13	100	Portal-of-entry (oral)
Pyrene (129-00-0)	3	NOAEL	75	7	75	100	Kidney
Benzo[a]pyrene (50-32-8)	3	BMDL	0.092	7	0.092	100	Neurodevelopmental
2-Methylnaphthalene (91-57-6)	3	BMDL	3.5	7	3.5	100	Pulmonary alveolar proteinosis
1,3-Pentadiene (504-60-9)	3	NOEL	100	7	100	100	Transient decrease in maternal food intake

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table 17. Non-cancer Inhalation PODs for Analogous Mixtures (Tier 2) and Worst Case Constituents (Tier 3)								
Analogous Mixture or Worst Case Constituent (CASRN)	**Tier**	**POD Type**	**POD (mg/m3)**	**POD Exposure Time (hr/d)**	**POD Exposure Frequency (hr/d)**	**Adjusted POD (mg/m3)**	**Benchmark Margin of Exposure**	**Endpoint**
64741-41-9	2	NOAEC	2370	6	5	423	100	Liver, thyroid, decreased body weight
64741-55-5	2	NOAEC	2200	6	5	411	100	Developmental toxicity
64741-66-8	2	NOAEC	24,300	6	5	4339	100	None
64741-68-0	2	NOAEC	2810	6	5	502	100	Mortality and lung toxicity
64742-47-8	2	NOAEC	100	6	5	18	100	None
isobutane/2-methylbutane mixture (50:50)	2	NOAEC	13,500	6	5	2411	100	None
Commercial hexane (no CASRN)	2	NOAEC	877	22	7	804	100	Decreased body weight and neurotoxicity
1-Methylnaphthalene (90-12-0)	3	LOAEC	3	6	5	0.54	1000	Nasal lesions
2-Methylpentane (107-83-5)	3	LOAEC	5300	9	5	1420	1000	Decreased body weight
Dicyclopentadiene (77-73-6)	3	NOAEC	0.97	24	7	0.97	100	Kidney
Benzene (71-43-2)	3	BMCL	8.2	24	7	8.2	10	Decreased lymphocyte count
Benzo[a]pyrene (50-32-8)	3	LOAEC	0.025	4	7	0.0042	1000	Decreased embryo/fetal survival
2-methylpropene (115-11-7)	3	NOAEC	4589	6	5	819	100	Nasopharyngeal histopathology changes

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table 18. Non-cancer Dermal PODs for Analogous Mixtures (Tier 2)					
Analogous Mixture (CASRN)	**POD Type**	**POD (mg/kg/day)**	**POD Exposure Frequency (d/wk)**	**Benchmark Margin of Exposure**	**Endpoint**
64741-55-5	NOAEL	300	5	100	No systemic effects
64741-59-9	NOAEL	25	5	100	Thymus
64741-66-8	NOAEL	2000	3	100	No systemic effects
64741-68-0	NOAEL	797	5	100	No systemic effects
64741-78-2	NOAEL	375	5	100	No systemic effects
64742-05-8	LOAEL	5	5	1000	Hematological/ Immune
64741-62-4	NOAEL	0.05	7	100	Developmental and maternal body weight
68334-30-5	NOAEL	50	7	100	Maternal body weight and vocalizations

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Cancer:

EPA identified oral slope factors for four aromatic constituents (benzene, benzo(a)pyrene, 1,1-biphenyl, and 1-methylnaphthalene). Table 19 shows the available oral cancer slope factors.

Table 19. Cancer Oral Slope Factors (OSFs) for Constituents (Tier 3)

Constituent (CASRN)	PIONA Class	Carbon Number	No. Aromatic Rings	OSF (per mg/kg/d)	Reference
Benzene (71-43-2)	A	C6	1	0.055	IRIS
Benzo(a)pyrene (50-32-8)	A	C20	5	1	IRIS
1,1-Biphenyl (92-52-4)	A	C12	2	0.008	IRIS
1-Methylnaphthalene (90-12-0)	A	C11	2	0.029	PPRTV

For oral cancer risk assessment, there were no Tier 2 analogous mixtures with oral slope factors, so Tier 3 constituents were used where applicable. For P-21-0144, 0147, 0148, and 0150, benzene is expected to be present at low concentrations ([redacted] to [redacted] of the mixture; see Table 2). For these cases, the benzene OSF was used to assess the oral cancer risk associated with the fraction of the mixture represented by benzene.

As shown in Table 2, P-21-0155, 0156, 0157, and 0158 are not expected to contain benzene, but are expected to contain other 1-ring and 2-ring aromatics (all cases) and 3-ring aromatics (P-21-0155). There are two oral slope factors for 2-ring aromatics and none for 3-ring aromatics (or for 1-ring aromatics other than benzene). The oral slope factor for 1-methylnaphthalene is higher and therefore more conservative, so it was chosen as the basis for oral cancer risk assessment for mixtures like P-21-0146, 0155, 0156, 0157, and 0158 that are expected to include 2-ring aromatics in the C11-12 carbon range. Therefore, for these cases, the oral slope factor for 1-methylnaphthalene was used to assess the cancer risk associated with the expected fraction of 2-ring aromatic compounds in the NCSs ([redacted] to [redacted] see Table 2).

P-21-0146 is expected to contain up to [redacted] compounds. Based on the carbon range for this new chemical substance (C7-C12; see Table 1), it would not contain benzene (C6) but could contain 1-methylnaphthalene (C11); thus, the OSF for 1-methylnaphthalene was used to assess the cancer risk associated with the aromatic fraction.

P-21-0152 is not expected to contain [redacted] but is expected to contain [redacted] compounds and [redacted] compounds. There are no oral slope factors for 3- or 4-ring aromatic compounds. However, EPA's (1993) Provisional Guidance for Quantitative Risk Assessment of Polycyclic Aromatic Hydrocarbons shows relative potency factors (RPFs) for two [redacted]. No RPFs for 3-ring aromatics are available in the EPA (1993) document. The RPFs are combined with the slope factor or inhalation unit risk for benzo(a)pyrene (EPA 2017) to assess cancer risk. For P-21-0152, the RPF

[redacted]

for benz(a)anthracene (the more conservative of the RPFs for 4-ring aromatics) was used with the oral slope factor for benzo(a)pyrene to assess cancer risk from oral exposure.

P-21-0154 is not expected to contain benzene but is expected to contain other 1-ring aromatics as well as 2-, 3-, and 4-ring aromatics. For this case, the OSF for 1-methylnaphthalene was used to assess cancer risk for the 2-ring aromatic fraction, and the OSF for benzo(a)pyrene was used with the RPF for benz(a)anthracene to assess cancer risk for the 4-ring aromatic fraction. No OSF is available for a representative 3-ring aromatic.

For the remaining cases (P-21-0145, 0148, 153, 0160, 0161, 0162, and 0133) oral cancer risk was not assessed due to the lack of Tier 2 analogous mixtures or Tier 3 constituents with quantitative cancer information.

EPA identified inhalation unit risks (IURs) for two petroleum mixtures (commercial hexane and Stoddard Solvent IIC) and two aromatic constituents (benzene and benzo(a)pyrene), as shown in Table 20.

Table 20. Cancer Inhalation Unit Risks (IURs) for Analogous Mixtures (Tier 2) and Constituents (Tier 3)

Analogous Mixture or Constituent (CASRN)	Tier	PIONA Class(es)	Carbon Number	IUR (per µg/m3)	Reference
Commercial hexane (no CASRN)	2	PIN	C6	2.00E-07	PPRTV
Stoddard Solvent IIC (64742-88-7)	2	PIN	C10-C13	4.50E-06	PPRTV
Benzene (71-43-2)	3	A	C6	7.80E-06	IRIS
Benzo(a)pyrene (50-32-8)	3	A	C20	6.00E-04	IRIS

No quantitative estimates of cancer risk via dermal exposure were identified.

For inhalation cancer risk assessment, the IUR for commercial hexane or Stoddard Solvent IIC was used when one of these mixtures was identified as a Tier 2 analogue for the new chemical substance. For the following cases, inhalation cancer risks were evaluated using one of these mixtures: P-21-0147, 0150, and 0158. For the remaining cases, neither mixture was considered analogous. For P-21-0144 and 0148, benzene is expected to be present at low concentrations ([redacted] of the mixture; see Table 2). For these cases, the benzene IUR was used to assess the cancer risk associated with the fraction of the mixture represented by benzene.

P-21-0152 is not expected to contain benzene but is expected to contain [redacted] compounds and [redacted] compounds. There are no inhalation unit risks for 3- or 4-ring aromatic compounds. Similar to the approach described above for oral cancer assessment of this new chemical substance, the RPF for benz(a)anthracene was used with the inhalation unit risk for benzo(a)pyrene to assess cancer risk from inhalation exposure to P-21-0152.

[redacted]

For the remaining cases (P-21-0145, 0146, 149, 0153, 0155, 0156, 0157, 0160, 0161, 0162, and 0163) inhalation cancer risk was not assessed due to the lack of Tier 2 analogous mixtures or Tier 3 constituents with quantitative cancer information.

Table 21 summarizes the Tier 2 analogous mixtures and Tier 3 constituents used to assess oral and inhalation cancer risk for each new chemical substance. In the absence of quantitative cancer information for dermal exposure, cancer risk associated with this exposure route was assessed qualitatively.

[redacted]

Table 21. Summary of Tier 2 Analogous Mixtures and Tier 3 Constituents Used for Cancer PODs (P-21-0144 through P-21-0150)							
Case number	**P-21-0144**	**P-21-0145**	**P-21-0146**	**P-21-0147**	**P-21-0148**	**P-21-0149**	**P-21-0150**
Petroleum equivalent	**64741-54-4**	**64741-65-7**	**68527-27-5**	**64742-48-9**	**64741-55-5**	**64741-66-8**	**64742-49-0**
Basis for Oral Slope Factor							
Tier 2 Analogous Mixture	None identified	None identified	None identified	None identified	None identified	None identified	None identified
Tier 3 Constituent	[redacted]						
Basis for Inhalation Unit Risk							
Tier 2 Analogous Mixture	[redacted]						
Tier 3 Constituent							

Table 21 (Cont'd). Summary of Tier 2 Analogous Mixtures and Tier 3 Constituents Used for Cancer PODs (P-21-0152 through P-21-0157)						
Case number	**P-21-0152**	**P-21-0153**	**P-21-0154**	**P-21-0155**	**P-21-0156**	**P-21-0157**
Petroleum equivalent	**64741-62-4**	**64741-76-0**	**64742-59-2**	**64741-59-9**	**64742-38-7**	**64742-46-7**
Basis for Oral Slope Factor						
Tier 2 Analogous Mixture	None identified	None identified	None identified	None identified	None identified	None identified
Tier 3	[redacted]					

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table 21 (Cont'd). Summary of Tier 2 Analogous Mixtures and Tier 3 Constituents Used for Cancer PODs (P-21-0152 through P-21-0157)						
Constituent	[redacted]					
Basis for Inhalation Unit Risk						
Tier 2 Analogous Mixture	None identified	None identified	None identified	None identified	None identified	None identified
Tier 3 Constituent	[redacted]					

Table 21 (Cont'd). Summary of Tier 2 Analogous Mixtures and Tier 3 Constituents Used for Cancer PODs (P-21-0158, P-21-0160 through P-21-0163)					
Case number	**P-21-0158**	**P-21-0160**	**P-21-0161**	**P-21-0162**	**P-21-0163**
Petroleum equivalent	**64742-47-8**	**68477-85-0**	**68783-64-2**	**68478-12-6**	**68478-32-0**
Basis for Oral Slope Factor					
Tier 2 Analogous	None identified	None identified	None identified	None identified	None identified

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table 21 (Cont'd). Summary of Tier 2 Analogous Mixtures and Tier 3 Constituents Used for Cancer PODs (P-21-0158, P-21-0160 through P-21-0163)					
Mixture					
Tier 3 Constituent	[redacted]	None identified	None identified	None identified	None identified
Basis for Inhalation Unit Risk					
Tier 2 Analogous Mixture	Stoddard Solvent IIC	None identified	None identified	None identified	None identified
Tier 3 Constituent	NA	None identified	None identified	None identified	None identified

[redacted]

5.4 Human Health Hazard Language

Acute Toxicity, Skin Irritation, Eye Irritation, Carcinogenicity, Genetic Toxicity, Reproductive Toxicity, Specific Target Organ Toxicity, Aspiration Hazard

6 Use, Release and Exposure

For this assessment, US EPA assessed occupational exposure and environmental releases using the 5/12/2016 version of ChemSTEER. Input to ChemSTEER tool includes information from: the submission, physical / chemical properties, and relevant past cases. The NCSs are chemical intermediates for fuel products or are used themselves in fuels.

6.1 Uses

This integrated report consists of new chemicals P21-0144, 145, 146, 147, 148, 149, 150, 152, 153, 154, 155, 156, 157, 158, 160, 161, 162, and 163. The intended uses are as follows:

- P21-0144 – 148, 150: Fuel component in gasoline.
- P21-0149: Component of aviation gasoline.
- P21-0152: Component in marine fuels.
- P21-0153, 154, and 160-163: Chemical intermediate / refinery feedstock.
- P21-0155, 157: Fuel in diesel.
- P21-0156, 158: Jet fuel.

6.2 Environmental Releases

Per the Engineering Reports dated 2-2-2022 through 2-4-2022, the following environmental releases were estimated using a combination of the methods noted below:

- Submitter estimates: Where information is available, environmental release estimates from the submitter were evaluated and utilized for the submitter site (manufacturing site).
- EPA/OPPT models: Release models in ChemSTEER are used to estimate releases from industrial/commercial activities. Note certain standard models have a vapor pressure threshold of 35 torr; where such models are used to estimate fugitive air releases, the model input is capped at 35 torr to prevent overestimation. This results in a high level of uncertainty in the estimate.
- Federal and state regulations including EPA's effluent limitation guidelines and pretreatment standards in 40 CFR Subpart A and the Spill Prevention, Control, and Countermeasure (SPCC) regulations.
- EPA AP-42 Emission Factors for the transportation and marketing of petroleum liquids (Chapter 5.2) and for organic liquid storage tanks (Chapter 7).

Tables 22 through 31 present details of the activity, release quantity, environmental media, and basis for the release estimates for the manufacturing, processing, and uses of the NCSs.

[redacted]

Table 22. Environmental Release Sources for MFG

Activity	Media of Release	Basis for Release Estimates	Applicable Cases
Sampling Liquid Product	Air (unknown if stack or fugitive)	EPA/OPPT Penetration Model (capped at 35 torr). EPA uses the vapor generation rate per the model and the submission-specified activity time of 0.25 hrs/day to estimate this release.	144, 145, 146, 147, 148, 149, 150, 153, 154, 155, 156, 157, 158, 160, 161, 162, 163
Fugitive Emissions from Process	Fugitive Air	User-defined Vapor Generation Rate Model. Submission estimates [redacted] kg/day of fugitive emissions released from process. Submission estimates associated exposure occurs over [redacted] however, EPA assumes release occurs over [redacted] because release is from fugitive emissions.	All

Table 23. Environmental Release Summary for MFG

Activity	Release Quantity (kg/site-day)																	
	144	145	146	147	148	149	150	152	153	154	155	156	157	158	160	161	162	163
	[redacted]																	
Sampling Liquid Product (over [redacted] days/yr)	1.1 E-2	1.8 E-3	1.2 E-2	9.1 E-3	1.1 E-2	1.4 E-2	1.5 E-2	n/a	2.0 E-5	2.3 E-4	1.4 E-5	1.4 E-5	1.4 E-5	1.4 E-5	6.9 E-3	6.9 E-3	6.9 E-3	6.9 E-3
Fugitive Emissions (over [redacted] days/yr)	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1
RELEASE TOTAL (kg/yr – all sites)	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**	**3.6 E+2**	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**	**3.7 E+2**

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table 24. Environmental Release Sources for Processing 1: Blending

Activity	Media of Release	Basis for Release Estimates	Applicable Cases
Fugitive Emissions from Process	Fugitive Air	User-defined Vapor Generation Rate Model. Submission estimates [redacted] kg/day of fugitive emissions released from process. Submission estimates associated exposure occurs over [redacted]; however, EPA assumes release occurs over [redacted] because release is from fugitive emissions.	144, 145, 146, 147, 148, 149, 150, 152, 155, 156, 157, 158
Tank emissions	Fugitive Air	User-Defined Loss Rate Model. The submitter's data indicates a [redacted] of [redacted] kg VOC/tank-yr and a [redacted] of [redacted] kg VOC/tank-yr, and indicates the number of tanks that contain each NCS. EPA uses these values with the estimated concentration of NCS in vapor (calculated based on molecular weight, vapor pressure, concentration in the liquid, and surrogate chemical data) to estimate this release. This release is expected to be through vents on the tank roof.	144, 145, 146, 147, 148, 149, 150, 155, 156, 157, 158
Loading Liquid Product into Tank Trucks	Fugitive Air Other (recycled / recovered)	User-Defined Loss Rate Model. EPA calculated loading losses using AP-42 Section 5.2 for the transportation and marketing of petroleum liquids, assuming a saturation factor of 1, a temperature of 77 degrees, and an estimated weight fraction of NCS in the vapor (calculated based on molecular weight, vapor pressure, concentration in the liquid, and surrogate chemical data). Submitter estimates a vapor recovery system with 99.999% efficiency, but regulations generally require the use of a vapor recovery system with at least 95% efficiency. Therefore, EPA assesses 95% capture and recovery (recycled) in vapor recovery system.	155, 156, 157, 158
Cleaning Liquid Residuals from Tank Trucks Used to Transport the Raw Material	Water or Incineration or Landfill Incineration or Landfill	EPA/OPPT Bulk Transport Residual Model, CEB standard 0.2% residual. Submission indicates cleaning is done by a third party with an estimated annual frequency and release to incineration or landfill, per regulations which restrict the disposal to wastewater. While the heel is collected and not usually disposed to water, there is a possibility for annual cleaning to water per EPA's effluent limitation guidelines and pretreatment standards in Subpart A of 40 CFR Part 442. Therefore, NEPA estimates the Central Tendency loss fraction (LF = [redacted]) to incineration, landfill or water and the rest to landfill or incineration [redacted].	152
Equipment Cleaning Losses of Liquids from Multiple Vessels	Water or Incineration or Landfill	EPA/OPPT Multiple Process Vessel Residual Model, CEB standard 2% residual. API Standard 653 requires internal inspections of petroleum storage tanks at least every 10 years, at which time the tanks must be cleaned. EPA assumes annual cleaning using	152

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

Activity	Media of Release	Basis for Release Estimates	Applicable Cases
		the EPA/OPPT Multiple Process Vessel Residual Model. During cleaning, tanks are emptied with a vacuum hose and cleaned with pressurized water, which is also removed with a vacuum hose. SPCC regulations at 40 CFR Part 112 prevent the release of petroleum products to surface waters; therefore, any equipment cleaning wastewater would first undergo treatment before discharge. Therefore, this release is assessed to wastewater treatment, landfill, or incineration.	

Table 25. Environmental Release Summary for Processing 1: Blending

Activity	Release Quantity (kg/site-day)																
	144	145	146	147	148	149	150	152			155	156	157	158	160	161	162	163
Fugitive Emissions (over [redacted] days/yr)	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1			10.0 E-1	10.0 E-1	10.0 E-1	10.0 E-1				
Tank Emissions (over [redacted] days/yr)	1.1 E-1	6.2 E-4	1.2 E-2	8.8 E-2	2.7 E+0	1.3 E-1	3.0 E-1	n/a			7.3 E-4	1.3 E-4	1.5 E-3	3.6 E-4				
Loading Liquid Product into Tank Trucks (Air) (over [redacted] days/yr)	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	3.2 E-2	7.3 E-3	6.2 E-2	4.8 E-2	n/a	n/a	n/a	n/a
Loading Liquid Product into Tank Trucks (Other) (over [redacted] days/yr)	n/a	n/a	n/a	n/a	n/a	n/a	n/a				6.1 E-1	1.4 E-1	1.2 E+0	9.2 E-1				

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

Activity	Release Quantity (kg/site-day)																
Cleaning Liquid Residuals from Tank Trucks (Water, Incineration, Land) [redacted]	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2.7 E+2			n/a	n/a	n/a	n/a			
Cleaning Liquid Residuals from Tank Trucks (Incineration, Land [redacted]	n/a	n/a	n/a	n/a	n/a	n/a	n/a	5.1 E+2			n/a	n/a	n/a	n/a			
Equipment cleaning [redacted]	n/a	n/a	n/a	n/a	n/a	n/a	n/a	7.8 E+3			n/a	n/a	n/a	n/a			
RELEASE TOTAL (kg/yr – all sites)	**4.0 E+2**	**3.7 E+2**	**3.7 E+2**	**4.0 E+2**	**1.4 E+3**	**4.1 E+2**	**4.7 E+2**	**9.0 E+3**			**6.0 E+2**	**4.2 E+2**	**8.2 E+2**	**7.2 E+2**			

Table 26. Environmental Release Sources for Processing 2: Loading at Bulk Terminals

Activity	Media of Release	Basis for Release Estimates	Applicable Cases
Equipment Cleaning Losses of Liquids from Multiple Vessels	Water or Incineration or Landfill	EPA/OPPT Multiple Process Vessel Residual Model, CEB standard 2% residual. API Standard 653 requires internal inspections of petroleum storage tanks at least every 10 years, at which time the tanks must be cleaned. EPA assumes annual cleaning using the EPA/OPPT Multiple Process Vessel Residual Model. During cleaning, tanks are emptied with a vacuum hose and cleaned with pressurized water, which is also removed with a vacuum hose. SPCC regulations at 40 CFR Part 112 prevent the release of petroleum products to surface waters; therefore, any equipment cleaning wastewater would first undergo treatment before discharge. Therefore, this release is assessed to wastewater treatment, landfill, or incineration.	144, 145, 146, 147, 148, 149, 150

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

Activity	Media of Release	Basis for Release Estimates	Applicable Cases
	Fugitive Air	EPA/OPPT Mass Transfer Coefficient Model (capped at 35 torr).	
Loading Liquid Product into Tank Trucks	Fugitive Air	User-Defined Loss Rate Model. EPA calculated loading losses using AP-42 Section 5.2 for the transportation and marketing of petroleum liquids, assuming a saturation factor of 1, a temperature of 77 degrees, and an estimated weight fraction of NCS in the vapor (calculated based on molecular weight, vapor pressure, concentration in the liquid, and surrogate chemical data). Regulations generally require the use of a vapor recovery system with at least 95% efficiency. Therefore, EPA assesses 95% capture and recovery (recycled) in vapor recovery system.	144, 145, 146, 147, 148, 149, 150
	Other (recycled / recovered)		
Tank Standing/ Working Losses	Fugitive Air	User-Defined Loss Rate Model. EPA expects there are emissions from fuel storage tanks at terminals. EPA estimates this release using AP-42 methodology, assuming 110 ft diameter/50 ft tall tanks (with [redacted] gal/yr throughput with [redacted] turnovers), Key West FL (due to unknown terminal location for the region), internal floating roof tanks, and other default assumptions. EPA estimates the number of tanks/site using the NCS PV and concentration in gasoline. This release is expected to be through vents on the tank roof.	144, 145, 146, 147, 148, 149, 150
Sampling Liquid Product	Fugitive Air	EPA/OPPT Penetration Model (capped at 35 torr).	144, 145, 146, 147, 148, 149, 150

Table 27. Environmental Release Summary for Processing 2: [redacted]

Activity	Release Quantity (kg/site-day)																	
	144 [redacted]	145 [redacted]	146 [redacted])	147 [redacted]	148 ([redacted])	149 [redacted])	150 [redacted])	152	153	154	155	156	157	158	160	161	162	163
Equipment cleaning (Water, Incineration, Landfill) (over 1	1.2E+2	1.2E+2	2.4E+1	7.2E+1	1.0E+3	4.2E+2	7.2E+1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Activity	Release Quantity (kg/site-day)
day/yr)	[redacted]
Equipment cleaning (Air) [redacted]	
Loading Liquid Product into Tank Trucks (Air) (over [redacted] days/yr)	
Loading Liquid Product into Tank Trucks (over [redacted] days/yr) (Other)	
Tank Standing/ Working Losses (over [redacted] days/yr)	
Sampling Liquid Product (over [redacted] days/yr)	
RELEASE TOTAL (kg/yr – all	

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Activity	Release Quantity (kg/site-day)																	
sites)																		

Table 28. Environmental Release Sources for Use: Fuel

Activity	Media of Release	Basis	Applicable Cases
Cleaning Liquid Residuals from Tank Trucks Used to Transport the Raw Material	Water or Incineration or Landfill	EPA/OPPT Bulk Transport Residual Model, CEB standard 0.2% residual. Submission indicates cleaning is done by a third party with an estimated annual frequency and release to incineration or landfill, per regulations which restrict the disposal to wastewater. While the heel is collected and not usually disposed to water, there is a possibility for annual cleaning to water per EPA's effluent limitation guidelines and pretreatment standards in Subpart A of 40 CFR Part 442. Therefore, NEPA estimates the Central Tendency loss fraction (LF = [redacted]) to incineration, landfill or water and the rest to landfill or incineration ([redacted]).	144, 145, 146, 147, 148, 149, 150, 152, 155, 156, 157, 158
	Incineration or Landfill		
	Fugitive Air	EPA/OPPT Mass Transfer Coefficient Model (capped at 35 torr)	
Unloading Liquid Raw Material from Tank Trucks	Fugitive Air	User-Defined Loss Rate Model. EPA calculates loading losses using AP-42 Section 5.2 for gasoline service station operations and an estimated weight fraction of NCS in the vapor (calculated based on molecular weight, vapor pressure, concentration in the liquid, and surrogate chemical data). This approach assumes a mix of submerged filling, splash filling, and vapor balanced filling, with the addition of underground tank breathing and emptying.	144, 145, 146, 147, 148, 149, 150, 152, 155, 156, 157, 158
Incineration	Incineration	User-Defined Loss Rate Model. Fuel is combusted in engines. EPA assesses 100% release of the NCS and subtracts upstream losses to estimate the loss fraction for this release. This release only accounts for the industrial/commercial use portion of the NCS.	144, 145, 146, 147, 148, 149, 150, 152, 155, 156, 157, 158

[redacted]

Table 29. Environmental Release Summary for Use: Fuel

Activity	Release Quantity (kg/site-day)																	
	144 [redacted] sites)	145 [redacted] sites)	146 [redacted] sites)	147 [redacted] sites)	148 [redacted]	149 [redacted] sites)	150 [redacted]	152 [redacted] sites)	153	154	155 [redacted] sites)	156 [redacted]	157 [redacted] sites)	158 [redacted] sites)	160	161	162	163
Cleaning Liquid Residuals from Tank Trucks (Water, Incineration, Land) [redacted] day/yr)	[redacted]																	
Cleaning Liquid Residuals from Tank Trucks (Incineration, Land) [redacted] day/yr)	[redacted]																	
Cleaning Liquid Residuals from Tank Trucks (Air) [redacted]	[redacted]																	
Unloading (over [redacted] day/yr)	[redacted]																	
Incineration (over [redacted] day/yr)	[redacted]																	
RELEASE TOTAL (kg/yr – all sites)	[redacted]																	

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table 30. Environmental Release Sources for Use: Chemical Intermediate

Activity	Media of Release	Basis	Applicable Cases
Fugitive Emissions from Process	Fugitive Air	User-defined Vapor Generation Rate Model. Submission estimates [redacted] kg/day of fugitive emissions released from process. Submission estimates associated exposure occurs [redacted] hr/day; however, EPA assumes release occurs over 24 hr/day because release is from fugitive emissions.	153, 154, 160, 161, 162, 163
Tank Emissions	Fugitive Air	User-Defined Loss Rate Model. The submitter's data indicates a [redacted] of [redacted] kg VOC/tank-yr and a [redacted] of [redacted] kg VOC/tank-yr, and indicates the number of tanks that contain each NCS. EPA uses these values with the estimated concentration of NCS in vapor (calculated based on molecular weight, vapor pressure, concentration in the liquid, and surrogate chemical data) to estimate this release. This release is expected to be through vents on the tank roof.	153, 154

Table 31. Environmental Release Summary for Use: Chemical Intermediate

Activity	Release Quantity (kg/site-day)																	
	144	145	146	147	148	149	150	152	153 [redacted]	154 [redacted]	155	156	157	158	160 [redacted]	161	162	163
Fugitive Emissions (over [redacted] day/yr)	[redacted]																	
Tank Emissions (over [redacted] day/yr)	[redacted]																	
RELEASE TOTAL (kg/yr – all sites)	[redacted]																	

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

6.3 Exposures

EPA estimated worker exposures using EPA/OPPT models in ChemSTEER and monitoring data, where available.

6.3.1 Worker Exposure

Per Engineering Reports dated 2/3/2022 and 2/4/2022

Worker exposure estimates are summarized in Tables 32 through 35.

[redacted]

Table 32. Worker Exposure Estimates for P-21-0144 through P-21-0150							
Scenario and Dose	**P-21-0144**	**P-21-0145**	**P-21-0146**	**P-21-0147**	**P-21-0148**	**P-21-0149**	**P-21-0150**
Inhalation							
MFG: [redacted]							
Worker Inhalation Exposure (Scenario 1)							
Exposure to Vapor (volatile) (Class II)							
Output 2 PDR (mg/day over [redacted]):	1.80E+01	2.70E-01	2.60E+01	1.80E+01	6.20E+01	3.50E+00	6.00E+01
Output 2 LADC (µg/m^3 over [redacted]):	2.07E+02	3.13E+00	2.95E+02	2.07E+02	7.03E+02	4.03E+01	6.86E+02
PROC1: Blending							
Worker Inhalation Exposure (Scenario 2)							
Exposure to Vapor (volatile) (Class II)							
Output 2 PDR (mg/day over [redacted]	5.70E-01	8.30E-03	1.60E-01	3.40E-01	1.90E+01	3.50E+00	1.30E+00
Output 2 LADC (µg/m^3 over [redacted]):	6.49E+00	9.47E-02	1.80E+00	3.84E+00	2.14E+02	4.03E+01	1.52E+01
PROC2: Loading at Bulk Terminals							
Loading Liquid Product into Tank Trucks (Scenario 3)							
Exposure to Vapor (volatile) (Class II)							
Worst Case PDR (mg/day [redacted] days/yr):	3.90E+00	5.80E-02	1.10E+00	2.30E+00	1.30E+02	2.40E+01	9.10E+00
Worst Case LADC (µg/m^3 [redacted] days/yr):	4.47E+01	6.56E-01	1.24E+01	2.65E+01	1.44E+03	2.76E+02	1.04E+02
Tank Standing/Working Losses (Scenario 4)							
Exposure to Vapor (volatile) (Class II)							
Output 2 PDR (mg/day over [redacted]	2.80E-01	8.30E-03	1.70E-01	1.70E-01	9.10E+00	4.00E-01	6.60E-01
Output 2 LADC (µg/m^3 over [redacted]	3.23E+00	9.46E-02	1.93E+00	1.91E+00	1.04E+02	4.59E+00	7.52E+00
Sampling Liquid Product (Scenario 5)							
Exposure to Vapor (volatile) (Class II)							

[redacted]

Worst Case PDR (mg/day [redacted] days/yr):	2.40E+00	4.00E-01	2.50E+00	2.00E+00	2.50E+00	3.00E+00	3.20E+00
Worst Case LADC (µg/m^3 [redacted] days/yr):	2.72E+01	4.59E+00	2.88E+01	2.27E+01	2.84E+01	3.42E+01	3.69E+01

USE: Fuel

Unloading Liquid Raw Material from Tank Trucks (Scenario 6)

Exposure to Vapor (volatile) (Class II)

Worst Case PDR (mg/day [redacted] days/yr):	3.60E+00	5.30E-02	9.90E-01	2.10E+00	1.20E+02	2.20E+01	8.30E+00
Worst Case LADC (µg/m^3 [redacted] /yr)	4.09E+01	6.05E-01	1.13E+01	2.42E+01	1.32E+03	2.52E+02	9.53E+01

Dermal

MFG: [redacted]

Sampling Liquid Product (Scenario 1)

Exposure to Liquid at concentration	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
High End PDR: (mg/day [redacted])	7.90E+01	3.90E+01	3.90E+01	7.90E+01	7.90E+01	3.90E+01	7.90E+01
High End LADD (mg/kg-day [redacted] days/yr)	3.50E-01	1.70E-01	1.70E-01	3.50E-01	3.50E-01	1.70E-01	3.50E-01

PROC1: Blending

Dermal exposure not expected from fugitive emissions.

PROC2: Loading at Bulk Terminals

Loading Liquid Product into Tank Trucks (Scenario 2)

Exposure to Liquid at concentration	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
High End PDR: (mg/day [redacted])	4.90E+00	2.50E+00	4.50E-01	2.90E+00	4.20E+01	7.90E+01	2.90E+00
High End LADD (mg/kg-day [redacted] days/yr)	2.20E-02	1.10E-02	2.00E-03	1.30E-02	1.90E-01	3.50E-01	1.30E-02

USE: Fuel

Unloading Liquid Raw Material from Tank Trucks (Scenario 3)

Exposure to Liquid at concentration:							
High End PDR (mg/day)	3.90E+00	1.90E+00	3.50E-01	2.30E+00	3.30E+01	6.20E+01	2.30E+00
High End LADD (mg/kg-day days/yr)	1.70E-02	8.50E-03	1.50E-03	1.00E-02	1.50E-01	2.70E-01	1.00E-02

Table 33. Worker Exposure Estimates for P-21-0152	
	P-21-0152
Inhalation	
MFG:	
Worker Inhalation Exposure (Scenario 1)	
Exposure to Vapor (volatile) (Class II)	
Output 2 PDR: (mg/day)	4.80E-06
Output 2 LADC (µg/m^3	5.47E-05
PROC: Blending	
Fugitive Emissions from Process (Scenario 2)	
Exposure to Vapor (volatile) (Class II)	
Worst Case PDR (mg/day)	7.30E-01
Worst Case (LADC): (µg/m^3)	8.32E+00
USE: Fuel	
Negligible (VP < 0.001 torr)	
Dermal	
MFG:	
Loading Liquid Product into Tank Trucks (scenario 1)	
Exposure to Liquid at concentration:	
High End PDR (mg/day)	1.60E+02

High End LADD (mg/kg-day [redacted])	6.90E-01
PROC: Blending	
Unloading Liquid Raw Material from Tank Trucks (Scenario 2)	
Exposure to Liquid at concentration:	[redacted]
High End PDR (mg/day [redacted])	1.60E+02
High End LADD (mg/kg-day [redacted])	6.90E-01
USE: Fuel	
Unloading Liquid Raw Material from Tank Trucks (Scenario 3)	
Exposure to Liquid at concentration:	[redacted]
High End PDR (mg/day [redacted])	1.60E+02
High End LADD (mg/kg-day [redacted])	6.90E-01

Table 34. Worker Exposure Estimates for P-21-0155 through P-21-0158

	P-21-0155	P-21-0156	P-21-0157	P-21-0158
Inhalation				
MFG: [redacted]				
Worker Inhalation Exposure (Scenario 1)				
Exposure to Vapor (volatile) (Class II)				
Output 2 PDR: (mg/day [redacted])	3.10E-02	1.30E-02	1.80E-02	5.00E-03
Output 2 LADC (µg/m^3 [redacted])	3.54E-01	1.48E-01	2.05E-01	5.71E-02
PROC: Blending				
Worker Inhalation Exposure (Scenario 2)				
Exposure to Vapor (volatile) (Class II)				
Output 2 PDR: (mg/day [redacted])	5.80E-03	7.70E-04	6.80E-03	2.00E-02
Output 2 LADC (µg/m^3 [redacted])	6.64E-02	8.79E-03	7.75E-02	2.28E-02

[redacted]

Loading Liquid product into Tank Trucks (Scenario 3)				
Exposure to Vapor (volatile) (Class II)				
Worst Case PDR: (mg/day [redacted])	3.90E-03	1.20E-03	4.60E-03	3.30E-03
Worst Case LADC (µg/m^3)	4.45E-02	1.40E-02	5.25E-02	3.72E-02
USE: Fuel				
Unloading Liquid Raw Material from Tank Trucks (Scenario 4)				
Exposure to Vapor (volatile) (Class II)				
Worst Case PDR: (mg/day [redacted])	3.60E-03	1.10E-03	4.20E-03	3.00E-03
Worst Case LADC (µg/m^3 [redacted]	4.11E-02	1.29E-02	4.79E-02	3.42E-02
Dermal				
MFG: [redacted]				
Sampling Liquid Product (Scenario 1)				
Exposure to Liquid at concentration	[redacted]	[redacted]	[redacted]	[redacted]
High End PDR: (mg/day [redacted])	7.90E+01	7.90E+01	4.70E+01	3.10E+01
High End LADD: (mg/kg-day [redacted]	3.50E-01	3.50E-01	2.10E-01	1.40E-01
PROC: Blending				
Loading Liquid Product into Tank Trucks (Scenario 2)				
Exposure to Liquid at concentration	[redacted]	[redacted]	[redacted]	[redacted]
High End PDR: (mg/day [redacted]	3.10E+01	9.90E+00	3.70E+01	2.60E+01
High End LADD: (mg/kg-day [redacted]	1.40E-01	4.30E-02	1.60E-01	1.10E-01
USE: Fuel				
Unloading Liquid Raw Material from Tank Trucks (Scenario 3)				
Exposure to Liquid at concentration	[redacted]	[redacted]	[redacted]	[redacted]
High End PDR: (mg/day [redacted]	2.50E+01	7.80E+00	2.90E+01	2.00E+01
High End LADD: (mg/kg-day [redacted]	1.10E-01	3.40E-02	1.30E-01	9.00E-02

[redacted]

Table 35. Worker Exposure Estimates for P-21-0153, P-21-0154, and P-21-0160 through P-21-0163						
	P-21-0153	P-21-0154	P-21-0160	P-21-0161	P-21-0162	P-21-0163
Inhalation						
MFG: [redacted]						
Worker Inhalation Exposure (Scenario 1)						
Exposure to Vapor (non-volatile) (Class II)						
Output 2 PDR (mg/day [redacted])	8.30E-01	5.20E+01	1.60E+01	1.60E+01	1.60E+01	1.60E+01
Output 2 LADC(µg/m^3 [redacted])	9.52E+00	5.90E+02	1.86E+02	1.86E+02	1.86E+02	1.86E+02
USE: Chemical Intermediate						
Worker Inhalation Exposure (Scenario 2)						
Exposure to Vapor (non-volatile) (Class II)						
Output 2 PDR (mg/day [redacted])	8.30E-01	5.20E+01	1.60E+01	1.60E+01	1.60E+01	1.60E+01
Output 2 LADC(µg/m^3 [redacted])	9.52E+00	5.90E+02	1.86E+02	1.86E+02	1.86E+02	1.86E+02
Dermal						
MFG: [redacted]						
Sampling Liquid Product (Scenario 1)						
Exposure to Liquid at concentration [redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
High End PDR:mg/day [redacted]	1.10E+00	7.90E+01	7.90E+01	7.90E+01	7.90E+01	7.90E+01
High End LADD:mg/kg-day [redacted]	4.90E-03	3.50E-01	3.50E-01	3.50E-01	3.50E-01	3.50E-01
USE: Chemical Intermediate						
Dermal exposure is not expected.						

[redacted]

6.3.2 General Population Exposure

Per Exposure Reports dated 2/9/22, 2/11/22, 2/18/22, and 2/23/22

General population exposure estimates are summarized in Table 36.

[redacted]

Table 36. Summary of General Population Exposure Estimates[a]								
Exposure	**Dose (mg/kg-day)**	**P-21-0144**	**P-21-0145**	**P-21-0146**	**P-21-0147**	**P-21-0148**	**P-21-0149**	**P-21-0150**
ORAL								
Drinking water, Adult	ADR	3.42E-2	3.42E-2	6.84E-3	2.05E-2	2.80E-1	1.20E-1	2.05E-2
	LADD	4.57E-6	4.57E-6	9.13E-7	2.74E-6	3.81E-5	1.60E-5	2.74E-6
Drinking water, Infant	ADR	3.42E-2	3.42E-2	6.84E-3	2.05E-2	2.80E-1	1.20E-1	2.05E-2
Fish Ingestion	ADR	8.34E+0	3.52E+1	1.70E-1	8.90E-1	1.94E+1	1.89E+3	1.28E+0
	LADD	2.60E-4	1.10E-3	5.40E-6	2.77E-5	6.04E-4	5.90E-2	3.98E-5
Groundwater impacted by landfill leachate	ADD	1.18E-4	9.27E-5	NA	7.06E-5	9.79E-4	4.11E-4	7.06E-5
	LADD	4.98E-5	3.93E-5	NA	2.99E-5	4.15E-4	1.74E-4	2.99E-5
INHALATION								
Fugitive Air	ADR	8.40E-3	8.19E-4	4.57E-3	2.07E-3	7.81E-2	1.06E-2	1.16E-2
	LADD	9.38E-4	3.23E-4	5.78E-4	8.17E-4	3.03E-2	3.23E-4	2.27E-3
	(µg/m3)	1.06E+1	3.66E+0	6.55E+0	9.26E+0	3.43E+2	3.66E+0	2.57E+1
Stack Air	ADR	No releases to stack air	No releases to stack air	No releases to stack air	No releases to stack air	No releases to stack air	3.09E+0	No releases to stack air
	LADD						2.60E-1	
	(µg/m3)						3.37E+3	
Exposure	**Dose (mg/kg-day)**	**P-21-0152**	**P-21-0153**	**P-21-0154**	**P-21-0155**	**P-21-0156**	**P-21-0157**	**P-21-0158**
ORAL								
Drinking water, Adult	ADR	6.82E+0	No releases to water	No releases to water	4.84E-3	1.25E-3	9.40E-3	8.26E-3
	LADD	5.81E-4			6.47E-7	1.67E-7	1.26E-6	1.10E-6
Drinking water, Infant	ADR	6.82E+0			4.84E-3	1.25E-3	9.40E-3	8.26E-3
Fish Ingestion	ADR	5.62E+4	No releases to water	No releases to water	1.21E+2	3.13E+1	4.91E+2	1.20E+3
	LADD	1.75E+0			3.77E-3	9.76E-4	1.53E-2	3.75E-2

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table 36. Summary of General Population Exposure Estimates[a]								
Groundwater impacted by landfill leachate	ADD	NA	No releases to landfill	No releases to landfill	No releases to landfill	9.82E-6	3.26E-5	6.42E-5
	LADD	NA				4.16E-6	1.38E-5	2.72E-5
INHALATION								
Fugitive Air	ADR	3.84E-4	8.02E-4	1.30E-3	7.80E-4	7.70E-4	7.91E-4	7.86E-4
	LADD	1.51E-4	3.16E-4	5.14E-4	3.07E-4	3.04E-4	3.12E-4	3.10E-4
	(µg/m3)	1.71E+0	3.58E+0	5.83E+0	3.49E+0	3.44E+0	3.54E+0	3.51E+0
Stack Air	ADR	1.06E+1	No releases to stack air	No releases to stack air	2.71E+1	7.78E+0	5.19E+1	5.19E+1
	LADD	4.10E-1			2.29E+0	6.60E-1	4.37E+0	4.37E+0
	(µg/m3)	5.24E+3			2.96E+4	8.49E+3	5.65E+4	5.65E+4

Exposure	Dose (mg/kg-day)	P-21-0160	P-21-0161	P-21-0162	P-21-0163
ORAL					
Drinking water		No releases to water			
Fish Ingestion		No releases to water			
Groundwater impacted by landfill leachate		No releases to landfill			
INHALATION					
Fugitive Air	ADR	7.68E-4	7.68E-4	7.68E-4	7.68E-4
	LADD	3.03E-4	3.03E-4	3.03E-4	3.03E-4
	(µg/m3)[b]	3.43E+0	3.43E+0	3.43E+0	3.43E+0
Stack Air		No releases to stack air			

[a]The highest ADR or LADD was selected for use in risk calculations.
[b]The fugitive air concentration used in cancer risk calculations is the estimated annual average concentration. This value may overestimate exposures for individuals who may be exposed for a duration less than the average lifetime of 80 years.

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

6.3.3 Consumer Exposure

Per Exposure Reports dated 2/9/22, 2/11/22, 2/18/22, and 2/23/22

6.3.3.1 Dermal

Consumer exposures via dermal contact were identified for P-21-0144 through P-21-0150 and P-21-0155 through P-21-0158. Consumer uses were not identified for the remaining cases. Table 37 shows the dermal exposure estimates for consumers.

Table 37. Summary of Consumer Dermal Exposure Estimates

Case	Scenario	New Chemical Substance weight fraction	ADR (mg/kg/day)	LADD (mg/kg/day)
P-21-0144	CEM[1] Liquid fuels/motor oil	[redacted]	3.81E-1	3.91E-3
P-21-0145	CEM[1] Gasoline		3.81E-1	3.91E-3
P-21-0146	CEM[1] Gasoline		3.47E-2	3.55E-4
P-21-0147	CEM[2] Gasoline		2.25E-1	2.31E-3
P-21-0148	CEM[1] Gasoline		2.25E-1	2.31E-3
P-21-0149	CEM[1] Liquid fuels/motor oil		6.07E+0	6.21E-2
P-21-0150	CEM[1] Liquid fuels/motor oil		2.25E-1	2.31E-3
P-21-0155	CEM[1] Liquid fuels/motor oil		2.43E+0	2.49E-2
P-21-0156	CEM[1] Liquid fuels/motor oil		7.63E-1	7.81E-3
P-21-0157	CEM[1] Liquid fuels/motor oil		2.83E+0	2.89E-2
P-21-0158	CEM[1] Liquid fuels/motor oil		2.01E+0	2.06E-2
P-21-0152, P-21-0153, P-21-0154, P-21-0160, P-21-0161, P-21-0162, P-21-0163: Consumer uses were not identified				

7 ENVIRONMENTAL AND HUMAN HEALTH RISK ASSESSMENT

7.1 Environmental Risks

Risks to the environment were evaluated by comparing estimated surface water concentrations (SWCs) with the acute and chronic concentrations of concern (COCs). When evaluating risks from chronic exposures, the number of the days of exceedance (SWC > chronic COC) is also considered in the risk assessment. As shown in Table 38 below, risks from acute exposures to the environment

[redacted]

were identified for P-21-0144, 0145, 0146, 0147, 0149, 0150 (during processing); for P-21-0155, 0156, 0157, and 0158 (during use); and for P-21-0148 and 0152 (during processing and use). Risks from acute exposures to the environment were not identified for P-21-0153, 0154, 0160, 0161, 0162, or 0163 because there were no releases to water. Risks from chronic exposures to the environment were not identified due to the lack of chronic releases to water or lack of any releases to water.

Table 38. Summary of Environmental Risks

Case	Acute Risks	Chronic Risks
P-21-0144	**Risks identified** (7Q10 SWC exceeded COC during processing)	Not identified (no chronic releases to water)
P-21-0145	**Risks identified** (7Q10 SWC exceeded COC during processing)	Not identified (no chronic releases to water)
P-21-0146	**Risks identified** (7Q10 SWC exceeded COC during processing)	Not identified (no chronic releases to water)
P-21-0147	**Risks identified** (7Q10 SWC exceeded COC during processing)	Not identified (no chronic releases to water)
P-21-0148	**Risks identified** (7Q10 SWC exceeded COC during processing and use)	Not identified (no chronic releases to water)
P-21-0149	**Risks identified** (7Q10 SWC exceeded COC during processing)	Not identified (no chronic releases to water)
P-21-0150	**Risks identified** (7Q10 SWC exceeded COC during processing)	Not identified (no chronic releases to water)
P-21-0152	**Risks identified** (7Q10 SWC exceeded COC during processing and use)	Not identified (no chronic releases to water)
P-21-0153	Not identified (no releases to water)	Not identified (no releases to water)
P-21-0154	Not identified (no releases to water)	Not identified (no releases to water)
P-21-0155	**Risks identified** (7Q10 SWC exceeded COC during use)	Not identified (no chronic releases to water)

[redacted]

Table 38. Summary of Environmental Risks		
P-21-0156	**Risks identified** (7Q10 SWC exceeded COC during use)	Not identified (no chronic releases to water)
P-21-0157	**Risks identified** (7Q10 SWC exceeded COC during use)	Not identified (no chronic releases to water)
P-21-0158	**Risks identified** (7Q10 SWC exceeded COC during use)	Not identified (no chronic releases to water)
P-21-0160	Not identified (no releases to water)	Not identified (no releases to water)
P-21-0161	Not identified (no releases to water)	Not identified (no releases to water)
P-21-0162	Not identified (no releases to water)	Not identified (no releases to water)
P-21-0163	Not identified (no releases to water)	Not identified (no releases to water)

7.2 Human Health Risks

Risks to human health were evaluated using the PODs identified in Section 5.3 and exposure estimates reported in Section 6. Sections 7.2.1, 7.2.2, and 7.2.3 below summarize risk conclusions for workers, the general population, and consumers, respectively.

7.2.1 Worker Risks

Table 39 provides a summary of worker risk conclusions for each case. As the table shows, non-cancer risks were identified for inhalation exposures to P-21-0144, P-21-0146, P-21-0148, P-21-0152, P-21-0154, P-21-0155, P-21-0156, and P-21-0157. Non-cancer risks were identified for dermal exposures to P-21-0152, P-21-0153, P-21-0154, P-21-0155, and P-21-0156. Cancer risk estimates from inhalation exposure ranged between 1.9 E-09 and 3.1E-03. Cancer risk estimates from dermal exposure were not evaluated due to the lack of suitable POD for this exposure route.

Table 39. Summary of Worker Risks			
	Non-cancer Risks		**Cancer Risks**
Case	**Inhalation (Tier 2 or 3)**	**Dermal (Tier 2)**	**Inhalation (Tier 2 or 3)**
P-21-0144	**Risks identified** (MFG: Scenario 1; PROC2: Scenario 2; USE: Scenario 6)	Not identified	2.5E-08 to 1.6E-06
P-21-0145	Not identified	Not identified	POD not available
P-21-0146	**Risks identified** (MFG: Scenario 1; PROC2:	Not identified	POD not available

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table 39. Summary of Worker Risks			
	Scenario 5)		
P-21-0147	Not identified	Not identified	8.6E-06 to 9.3E-04
P-21-0148	**Risks identified** (MFG: Scenario 1, PROC: Scenarios 2, 3, 4, and 5; USE: Scenario 6)	Not identified	1.8E-06 to 9.0E-05
P-21-0149	Not identified	Not identified	POD not available
P-21-0150	Not identified	Not identified	3.3E-05 to 3.1E-03
P-21-0152	**Risks identified** (PROC: Scenario 2)	**Risks identified** (MFG: Scenario 1; PROC: Scenario 2; USE: Scenario 3)	1.3E-09 to 2.0E-04
P-21-0153	POD not available	**Risks identified** (MFG: Scenario 1)	POD not available
P-21-0154	**Risks identified** (MFG: Scenario 1; USE: Scenario 2)	**Risks identified** (MFG: Scenario 1)	7.1E-04
P-21-0155	**Risks identified** (MFG: Scenario 1)	**Risks identified** (MFG: Scenario 1)	POD not available
P-21-0156	**Risks identified** (MFG: Scenario 1)	**Risks identified** (MFG: Scenario 1)	POD not available
P-21-0157	**Risks identified** (MFG: Scenario 1)	Not identified	POD not available
P-21-0158	Not identified	POD not available	1.5E-07 to 2.6E-07
P-21-0160	Not identified	POD not available	POD not available
P-21-0161	Not identified	POD not available	POD not available
P-21-0162	Not identified	POD not available	POD not available
P-21-0163	Not identified	POD not available	POD not available

Respiratory, dermal, and eye irritation hazards to workers via inhalation and dermal contact were identified based on constituents of the NCSs. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards.

7.2.2 General Population Risks

Table 40 provides a summary of the non-cancer risks estimated for the general population.

[redacted]

For P-21-0144, 0148, 0149, 0150, 0152, and 0157, risks were identified for the general population (infants) for systemic and/or oral portal-of-entry effects via drinking water. Risks to adults for this exposure route were identified for P-21-0152. For P-21-0145, 0146, 0147, 0155, 0156, and 0158, risks were not identified for the general population for systemic and/or oral portal-of-entry effects via drinking water (adults or infants). For P-21-0153, 0154, 0160, 0161, 0162, and 0163, risks to the general population via drinking water were not evaluated because releases to surface water are not expected.

For P-21-0144, 0148, 0149, 0150, 0152, 0155, 0156, 0157, and 0158, risks were identified for the general population for systemic and/or oral portal-of-entry effects via fish ingestion. For P-21-0146 and 0147, risks were not identified for the general population for systemic and/or oral portal-of-entry effects via fish ingestion. For P-21-0153, 0154, 0160, 0161, 0162, and 0163, risks to the general population via fish ingestion were not evaluated because releases to surface water are not expected.

For P-21-0144, 0145, 0146, 0147, 0148, 0149, 0150, 0156, 0157, and 0158, risks were not identified for the general population for systemic and/or oral portal-of-entry effects via intake of groundwater impacted by landfill leachate. For P-21-0152, 0153, 0154, 0155, 0160, 0161, 0162, and 0163, risks to the general population via groundwater impacted by landfill leachate were not evaluated because releases to landfill were expected to be negligible (below modeling thresholds) or no releases are expected.

For P-21-0148, 0152, 0154, 0155, 0156, 0157 and 0158, risks were identified for the general population for systemic and/or inhalation portal-of-entry effects via fugitive air inhalation. For P-21-0144, 0145, 0146, 0147, 0149, 0150, 0160, 0161, 0162, and 0163, risks were not identified for the general population for systemic and/or inhalation portal-of-entry effects via fugitive air inhalation. For P-21-0153, there is insufficient information to assess hazard because of a lack of suitable Tier 2 mixtures or representative constituents with inhalation PODs. Therefore, EPA cannot make a risk determination for the general population exposed via fugitive air inhalation.

For P-21-0149, 0152, 0155, 0156, 0157 and 0158, risks were identified for the general population for systemic and/or inhalation portal-of-entry effects via stack air inhalation. For the remaining cases, risks to the general population via stack air inhalation were not evaluated because no releases are expected.

[redacted]

Table 40. Summary of General Population Non-Cancer Risks						
Case	**Drinking Water- Adult**	**Drinking Water- Infant**	**Fish Ingestion**	**Groundwater impacted by Landfill Leachate**	**Fugitive Air**	**Stack Air**
P-21-0144	Not identified	**Risks identified**	**Risks identified**	Not identified	Not identified	No releases expected
P-21-0145	Not identified	Not identified	**Risks identified**	Not identified	Not identified	No releases expected
P-21-0146	Not identified	Not identified	Not identified	Below modeling thresholds	Not identified	No releases expected
P-21-0147	Not identified	Not identified	Not identified	Not identified	Not identified	No releases expected
P-21-0148	Not identified	**Risks identified**	**Risks identified**	Not identified	**Risks identified**	No releases expected
P-21-0149	Not identified	**Risks identified**	**Risks identified**	Not identified	Not identified	**Risks identified**
P-21-0150	Not identified	**Risks identified**	**Risks identified**	Not identified	Not identified	No releases expected
P-21-0152	**Risks identified**	**Risks identified**	**Risks identified**	Below modeling thresholds	**Risks identified**	**Risks identified**
P-21-0153	No releases expected				POD not available	No releases expected
P-21-0154	No releases expected				**Risks identified**	No releases expected
P-21-0155	Not identified	Not identified	**Risks identified**	No releases expected	**Risks identified**	**Risks identified**
P-21-0156	Not identified	Not identified	**Risks identified**	Not identified	**Risks identified**	**Risks identified**
P-21-0157	Not identified	**Risks identified**	**Risks identified**	Not identified	**Risks identified**	**Risks identified**
P-21-0158	Not identified	Not identified	**Risks identified**	Not identified	**Risks identified**	**Risks identified**
P-21-0160	No releases expected				Not identified	No releases expected
P-21-0161	No releases expected				Not identified	No releases expected

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table 40. Summary of General Population Non-Cancer Risks			
P-21-0162	No releases expected	Not identified	No releases expected
P-21-0163	No releases expected	Not identified	No releases expected

Table 41 provides a summary of the cancer risks estimated for the general population. For the general population, cancer risk estimates for drinking water ranged between 1.3 E-10 (P-21-0146) and 2.3E-05 (P-21-0152). The cancer risk estimates for fish ingestion ranged between 2.7E-09 (P-21-0144) and 7.0E-02 (P-21-0152). The cancer risk estimates for consumption of groundwater impacted by landfill ranged between 2.7E-09 (P-21-0144) and 1.8E-07 (P-21-0148). The cancer risk estimates for inhalation of fugitive air ranged between 8.3E-8 (P-21-0144) and 1.2E-04 (P-21-0150). The exposure estimates for inhalation of stack air for P-21-0152 and P-21-0158 exceeded the PODs used for estimation of the IURs, so the IURs could not be used to estimate cancer risk. For these two cases, the cancer risks are estimated to be greater than 1E-01; which is extremely unlikely and reported here with high uncertainty.

Table 41. Summary of General Population Cancer Risks					
	Oral (Tier 3)				
Case	Drinking Water	Fish Ingestion	Groundwater Impacted by Landfill	Fugitive Air (Tier 2 or 3)	Stack Air (Tier 2 or 3)
P-21-0144	2.5E-10	1.4E-08	2.7E-09	8.3E-08	No releases expected
P-21-0145	POD not available	POD not available	POD not available	POD not available	No releases expected
P-21-0146	1.3E-10	7.8E-10	Below modeling thresholds	POD not available	No releases expected
P-21-0147	1.1E-09	1.1E-08	1.2E-08	4.2E-05	No releases expected
P-21-0148	1.7E-08	2.7E-07	1.8E-07	2.1E-05	No releases expected
P-21-0149	POD not available	POD not available	POD not available	POD not available	POD not available
P-21-0150	9.0E-10	1.3E-08	9.9E-09	1.2E-04	No releases expected
P-21-0152	2.3E-05	7.0E-02	Below modeling thresholds	4.1E-05	>1.0E-01 (High uncertainty)

[redacted]

Table 41. Summary of General Population Cancer Risks					
P-21-0153	No releases expected			POD not available	No releases expected
P-21-0154	No releases expected			7.0E-06	No releases expected
P-21-0155	9.4E-09	5.5E-05	No releases expected	POD not available	POD not available
P-21-0156	2.4E-10	1.4E-06	6.0E-09	POD not available	POD not available
P-21-0157	1.8E-09	2.2E-05	2.0E-08	POD not available	POD not available
P-21-0158	9.6E-10	3.3E-05	2.4E-08	1.6E-05	>1.0E-01 (High uncertainty)
P-21-0160	No releases expected			POD not available	No releases expected
P-21-0161	No releases expected			POD not available	No releases expected
P-21-0162	No releases expected			POD not available	No releases expected
P-21-0163	No releases expected			POD not available	No releases expected

Respiratory, dermal, and eye irritation hazards to the general population are not expected via drinking water ingestion, fish ingestion, groundwater impacted by landfill leachate, or fugitive or stack air releases due to dilution of the chemical substance in the media.

7.2.3 Consumer Risks

Consumer uses were identified for P-21-0144, 0145, 0146, 0147, 0148, 0149, 0150, 0155, 0156, 0157, and 0158. Consumer uses were not identified for the remaining cases. Table 42 provides a summary of consumer risks. Non-cancer risks to consumers via dermal contact were identified for P-21-0155 and not identified for any of the remaining cases. Cancer risks from dermal exposure were not quantified due to the lack of suitable POD for this exposure route.

Table 42. Summary of Consumer Risks from Dermal Exposure	
Case	Non-cancer (Tier 2)
P-21-0144	Not identified
P-21-0145	Not identified

[redacted]

Table 42. Summary of Consumer Risks from Dermal Exposure	
P-21-0146	Not identified
P-21-0147	Not identified
P-21-0148	Not identified
P-21-0149	Not identified
P-21-0150	Not identified
P-21-0155	**Risks identified**
P-21-0156	Not identified
P-21-0157	Not identified
P-21-0158	POD not available
P-21-0152, P-21-0153, P-21-0154, P-21-0160, P-21-0161, P-21-0162, P-21-0163	[redacted]

Respiratory, dermal, and eye irritation hazards to consumers via dermal contact were identified based on constituents of the new chemical substance. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards.

8 ASSUMPTIONS AND UNCERTAINTIES

Information submitted for the NCSs included names, definitions (including carbon ranges) and identification of the concurrently-produced [redacted] streams. The information submitted did not include identification of chemical constituents and approximate weight fraction for each. Further, the processes used to manufacture the NCSs will likely result in mixtures of varying composition. As a result, EPA has low confidence in the chemical composition of the new chemical substance. This adds a level of uncertainty to predictions of toxicity based on mixture composition, or when reading across from another [redacted] of variable composition (*i.e.,* an analogous mixture). In addition, as a complex mixture, there is uncertainty regarding the physical/chemical properties of the NCSs and only limited information was supplied by Chevron.

The assessments for environmental hazard and risk, and human health hazard and risk are based on available information for Tier 2 analogous mixtures, and information on constituents (Tier 3). The assessment for environmental fate used a weight of evidence approach using Tiers 2, 3 and 4 information. Information on analogous mixtures (Tier 2) may not adequately represent the new chemical substance, and information on individual constituents (Tier 3) will not reflect potential synergistic, antagonistic, or other interactions arising from the presence of multiple constituents within a mixture. Tier 4 information is based on prediction models and introduces more uncertainty into its use. In addition, for the human health hazard evaluation, physical chemical properties are often used to estimate absorption, and this does introduce uncertainty into that determination.

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

NCD considered identifying and assessing degradation products of the new chemical substance; however, NCD does not have adequate characterization of the NCSs to predict degradation products. There were some concerns regarding degradation of the NCSs resulting in more toxic constituents, but there is substantial uncertainty in predicting the nature and extent of toxic degradation products, because the composition of the NCSs is variable and its composition and fate in the environment will vary depending on local conditions. Potential degradation products and their toxic effects are a source of uncertainty in the assessment. This uncertainty in understanding the formation/identification of potential degradation products for the environmental fate analysis for such complex mixtures as the new chemical substance is challenging. Any potential method/model to better inform this would be useful.

EPA used modeling and estimation approaches to estimate environmental releases and worker exposures. Certain EPA/OPPT models have a vapor pressure threshold of 35 torr; where such models are used to estimate fugitive air releases and associated exposures, the model input is capped at 35 torr to prevent overestimation. This results in a high level of uncertainty in the estimate.

Where chemical-specific or site-specific information is not available, EPA used estimation methods and modeling approaches to estimate release and exposure, and applies engineering judgment where appropriate, There is some level of uncertainty associated with each method or model, including the use of surrogate monitoring data to assess inhalation exposure to truck drivers. Because of the high production volume and therefore high exposure estimates for the NCSs and their use, the uncertainty in the estimates may be reduced through targeted or focused monitoring efforts.

For the consumer exposure estimates, dermal exposure estimates were developed. The lack of consumer inhalation modeling for gasoline dispensing introduces an uncertainty resulting in an underestimation of the total exposure to consumers.

EPA assessed non-cancer oral and inhalation risks using both a Tier 2 mixture and a Tier 3 worst-case constituent where possible, to reduce the uncertainty in using either approach alone. However, as shown in Table 15, there are some cases that lacked a Tier 2 mixture with a POD for one or both routes, and some that lacked a Tier 3 worst-case constituent with a POD for one or both routes. Risk estimates for these cases are more uncertain.

Non-cancer oral PODs for three Tier 2 mixtures (CASRNs 64741-54-4, 64741-55-5, and 64741-66-8) were used to assess oral risks from the following cases: P-21-0144, 0145, 0146, 0148, and 0149. The study upon which the PODs were based (Halder et al. 1985) was focused on evaluating petroleum-induced nephropathy in male rats. The toxicological endpoints assessed were limited to mortality, clinical signs, body weight, gross necropsy, kidney weight, and kidney histopathology. The assessment of hazards based on PIONA class representative constituents, and the estimation of risks using the worst-case constituent serve to reduce the uncertainty associated with using PODs from this limited oral study.

[redacted]

A 104-week dermal carcinogenicity study of CASRN 64741-55-5, the petroleum equivalent analogue of P-21-0148, showed positive findings in mice, suggesting that this mixture is carcinogenic by this exposure route. Similarly, the petroleum equivalent for P-21-0155 (CASRN 64741-59-9) and the petroleum equivalent for P-21-0152 (CASRN 64741-62-4) each have several positive dermal carcinogenicity studies in mice. Due to limitations in available dermal carcinogenicity data, cancer risks from dermal exposure to these NCSs were evaluated qualitatively.

[redacted]

Appendix A: Approach Used to Evaluate Fuel-Stream Chemistries (from Renewable or Non-Renewable Sources)

Risk assessment of chemical mixtures is complicated by the presence of constituents with differing properties and potential toxic effects as well as the potential for interactions among the constituents that can alter the environmental fate, environmental hazard, and/or human health hazard of the mixture relative to its individual constituents. US EPA (2000, 1986) provides guidance for hazard assessment of chemical mixtures which includes a hierarchy of data preferences. In the hierarchy, experimentally-derived test data on the mixture of interest (in this case the new chemical substance) are preferred over data on sufficiently similar mixtures, followed by data on individual constituents if the first two options are not available.

Given that a robust chemical characterization, an understanding about environmental fate, and scientifically-defensible environmental/human health hazard information on a new chemical substance will not be common for these types of chemicals (Tier 1), this risk assessment approach will focus on the Tier 2 – determination of a "sufficiently similar mixture." As discussed in EPA (2000), "…sufficiently similar mixture refers to a mixture that is *very close in composition to the mixture of concern*, *such that differences in their components and their proportions are small*…". The document further states that a determination of sufficient similarity "should be made on a case-by-case basis, considering not only the uncertainties associated with using data on a surrogate mixture, but also contrasting the inherent uncertainties if one were to use other approaches, such as component-based methods".

The New Chemicals Division (NCD) will follow this established EPA guidance in a "case-by-case" approach. In addition, NCD is not prepared to identify criteria for "closeness" of a surrogate (or analogous) mixture to determine sufficient similarity. Rather, NCD recognizes there is a spectrum of possible mixtures for any given new chemical substance. Thus, any mixture being considered is an analogous mixture and its use as a sufficiently similar mixture may be different depending on the risk assessment discipline (i.e., chemistry, environmental fate, hazard, engineering, or exposure).

As previously stated, EPA (1986, 2000) recommends three approaches to the quantitative risk assessment of chemical mixtures, and when data for the mixture of concern or toxicologically similar/ analogous mixtures are unavailable, the third approach, Tier 3, is to evaluate the individual constituents. The goal of a constituent-based quantitative mixture assessment is to approximate the toxicity of the whole mixture by accounting for the toxicity of the individual constituents. EPA's Office of Pesticide Programs (OPP) has developed guidelines for the cumulative risk assessment of pesticide mixtures (OPP 2002) that begins with the identification of a group of chemicals with a common mechanism of toxicity (OPP 1999) and assesses the combined impacts of these mixture constituents. Consistent with the Agency's approach to multi-chemical assessments (EPA 1986 and 2000) that involve chemicals that are similar and share a common mechanism of toxicity, this OPP framework recommends the use of dose addition for determining the combined hazard and risk of the mixture.

The process described in these documents results in a highly refined cumulative risk assessment but requires an extensive amount of resources and toxicology data. The level of refinement provided by this approach is not necessary or even feasible for all new chemical submissions that may lack

[redacted]

adequate characterization (OPP 2015), and the OPP guidance (2002) also notes that not all cumulative assessments need to be of the same depth and scope. In specific circumstances (described below), a screening-level assessment may be employed, which applies more conservative approaches and overestimates of toxicity than would be made using the 2002 OPP guidance.

For the risk assessment of NCSs that are based on either renewable sources (biofuels) or other petroleum replacement substances (other, non-renewable sources), NCD is implementing a tiered approach for the evaluation of chemistry, environmental fate, environmental hazard, and human health hazard data based on this hierarchy, as shown below. At each tier, the suitability and quality of the data under consideration are evaluated, and data from multiple tiers may be used in a weight of evidence approach to ensure that the resulting assessment characterizes risks to human health and the environment and is based on the most reliable data available.

Multi-disciplinary Approach to Fuel-Stream Assessment

This tiered approach allows for flexibility and may be different for each new chemical substance, based on the information submitted, as submitters may propose analogous mixtures or major constituents, as well as other information found and used by NCD for that particular risk assessment.

Tier 1: Experimentally-derived data on the new chemical substance.

Tier 2: Experimentally-derived data on an analogous mixture.

Considerations for whether an analogous mixture is appropriate for use in the risk assessment of a new chemical substance that is being developed to blend with or replace a petroleum-based fuel, regardless of its source (renewable or not) include:

- Carbon chain length;
- Paraffinic, isoparaffinic, olefinic, naphthenic, and aromatic (PIONA) composition
- Physical-chemical properties (*e.g.,* physical state, boiling point, melting point, vapor pressure).

Other considerations include whether there are available data on representative constituents and/or constituents that will be the primary drivers of human health or environmental hazards. Data from this tier may be combined with data from Tier 3 to ensure that the resulting assessment protects human health and the environment and is based on the most reliable data available.

Consistent with EPA guidelines on mixture assessment, when data for the mixture of concern (Tier 1) or toxicologically similar/ analogous mixtures (Tier 2) are unavailable, the third approach is to evaluate the individual constituents.

Tier 3- Experimentally-derived data on the most prevalent and/or most toxic constituents of the new chemical substance (human health hazard and environmental fate).

Tier 3- Predicted (*in silico*) data on all constituents combined using the Toxic Unit approach (environmental hazard). The Toxic Unit approach, which predicts ecotoxicity endpoints for a mixture by combining the toxic contributions from each constituent, is provided in Appendix D.

[redacted]

Tier 4- Predicted (*in silico*) data on most prevalent constituents if no experimentally-derived data are available. Predictive tools (*e.g.,* EPISuite) will be used to fill data gaps for physical-chemical and environmental fate properties and other tools (*e.g.,* OECD QSAR Toolbox) will be used for human health hazard. .

Tier 4-Use of the most toxic individual constituents, based on either experimental data an/or predictions (*i.e.,* ECOSAR) and conservative assumptions in a screening-level assessment when mixture characterization is inadequate for higher tiered assessment (environmental hazard).

References for Appendix A

1. U.S. Environmental Protection Agency 1986. "Guidelines for the Health Risk Assessment of Chemical Mixtures". Risk Assessment Forum, U.S. Environmental Protection Agency, Washington DC. EPA/630/R-98/002.
2. U.S. Environmental Protection Agency. 1999. "Guidance for Identifying Pesticide Chemicals and Other Substances That Have a Common Mechanism of Toxicity". Office of Pesticide Programs, Office of Prevention, Pesticides, and Toxic Substances, Washington, D.C.
3. U.S. Environmental Protection Agency. 2000. "Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures". Risk Assessment Forum, U.S. Environmental Protection Agency, Washington DC. EPA/630/R-00/002.
4. U.S. Environmental Protection Agency. 2002. "Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity". Office of Pesticide Programs, Washington, D.C
5. U.S. Environmental Protection Agency. 2015. "Pesticide Cumulative Risk Assessment: Framework for Screening Analysis Purpose". Office of Pesticide Programs, Office of Chemical Safety and Pollution Prevention, Washington, D.C.

[redacted]

Appendix B: Environmental Fate Data

B.1 Environmental Fate Determination

Fate: Environmental fate is the determination of which environmental compartment(s) a chemical moves to, the expected residence time in the environmental compartment(s) and removal and degradation processes. Environmental fate is an important factor in determining exposure and thus in determining whether a chemical may present an unreasonable risk. NCD estimated physical/chemical and fate properties of the NCSs using data submitted for analogues, data for constituents ([redacted]) and EPI (Estimation Program Interface) Suite™ (http://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface). NCD estimated that the NCSs could have a range of ratings based on submitted analogue data, measured data for the constituents ([redacted]) and EPI Suite™ data. The submitted analogue data differed for each new chemical substance because each new chemical substance was made of varying compositions. Measured data were also found for constituents of the NCSs and were based on compositional information. In addition, the constituents were run in EPISuite™. A table containing the constituents and the analogue(s) utilized in the assessments is included below. In wastewater treatment, the NCSs are expected to be removed with an efficiency of 90% to 99% due to sorption, biodegradation, and/or stripping depending on the substance. Removal of the NCSs by biodegradation ranged from negligible to high. Sorption of the NCSs to sludge is expected to range from low to strong and to soil and sediment be expected to range from low to very strong. Migration of the NCSs to groundwater is expected to range from negligible to rapid due to low to very strong sorption to soil and sediment, depending on the new chemical substance. Due to variable estimated vapor pressures and Henry's law constants, the NCSs are expected to have a range of negligible to extensive volatilization to air. Overall, these estimates indicate that the NCSs may have potential to volatilize to air depending on the new chemical substance and low potential to migrate to groundwater.

Persistence[9]: Persistence is relevant to whether a new chemical substance is likely to present an unreasonable risk because chemicals that are not degraded in the environment at rates that prevent substantial buildup in the environment, and thus increase potential for exposure, may present a risk if the substance presents a hazard to human health or the environment. NCD estimated degradation half-lives of the NCSs using data submitted for analogues, data for constituents ([redacted]) and EPI Suite™. NCD estimated that the new chemical substance's aerobic and anaerobic biodegradation half-lives ranged from < 2 months to > 6 months and atmospheric oxidation by hydroxyl radical (OH•) ranged from slow to rapid, depending on the new chemical substance.

[9] Persistence: A chemical substance is considered to have limited persistence if it has a half-life in water, soil or sediment of less than 2 months or there are equivalent or analogous data. A chemical substance is considered to be persistent if it has a half-life in water, soil or sediments of greater than 2 months but less than or equal to 6 months or if there are equivalent or analogous data. A chemical substance is considered to be very persistent if it has a half-life in water, soil or sediments of greater than 6 months or there are equivalent or analogous data. (64 FR 60194; November 4, 1999)

[redacted]

Bioaccumulation[10]: Bioaccumulation is relevant to whether a new chemical substance is likely to present an unreasonable risk because substances that bioaccumulate in aquatic and/or terrestrial species pose the potential for elevated exposures to humans and other organisms via food chains. NCD estimated the potential for the NCSs to bioaccumulate using data for analogue(s) ([redacted]) and EPI Suite™. NCD estimated that the NCSs may have low to high bioaccumulation potential based on BCFBAF model results <1000, > 1000 to < 5000, and > 5000 across structures in the mixture. Since the NCSs are mixtures of hydrocarbons, the most conservative values were utilized in the assessments.

[10] Bioaccumulation: A chemical substance is considered to have a low potential for bioaccumulation if there are bioconcentration factors (BCF) or bioaccumulation factors (BAF) of less than 1,000 or there are equivalent or analogous data. A chemical substance is considered to be bioaccumulative if there are BCFs or BAFs of 1,000 or greater and less than or equal to 5,000 or there are equivalent or analogous data. A chemical substance is considered to be very bioaccumulative if there are BCFs or BAFs of 5,000 or greater or there are equivalent or analogous data. (64 FR 60194; November 4 1999)

PMN	P-21-0144	P-21-0145	P-21-0146	P-21-0147
Property	Chemical Identity			
Name	[redacted]			
CASRN				
Carbon range				
Data Sources	Analogue Biodegradation Data			
Hazard Characterization[1]	**Naphtha (petroleum), light alkylate, CASRN 64741-66-8; Naphtha (petroleum), heavy catalytic reformed, CASRN 64741- 63-5; Naphtha (petroleum), light catalytic cracked, CASRN 64741-55-5**: CONCAWE Inherent (CO2 Headspace) 42-96%/28 days.	**Naphtha (petroleum), light alkylate, CASRN 64741-66-8; Naphtha (petroleum), heavy catalytic reformed, CASRN 64741- 63-5; Naphtha (petroleum), light catalytic cracked, CASRN 64741-55-5**: CONCAWE Inherent (CO2 Headspace) 42-96%/28 days.	**Naphtha (petroleum), light alkylate, CASRN 64741-66-8; Naphtha (petroleum), heavy catalytic reformed, CASRN 64741- 63-5; Naphtha (petroleum), light catalytic cracked, CASRN 64741-55-5**: CONCAWE Inherent (CO2 Headspace) 42-96%/28 days.	**Naphtha (petroleum), light alkylate, CASRN 64741-66-8; Naphtha (petroleum), heavy catalytic reformed, CASRN 64741- 63-5; Naphtha (petroleum), light catalytic cracked, CASRN 64741-55-5**: CONCAWE Inherent (CO2 Headspace) 42-96%/28 days.
J-Check/NITE[2]	**m-xylene, CASRN 108-38-3:** Japanese MITI test: 30% by O2 consumption, 100% by GC and O2, GC and TOC; **1,3,5-trimethyl-benzene, CASRN 108-67-8:** Japanese MITI test: 0% by BOD and GC/28 days; **1-hexene, CASRN 592-41-6:** Japanese MITI test: 83% by BOD, 94% by TOC, 91% by GC/14 days	**n-nonane, CASRN 111-84-2:** Japanese MITI test: 96% by BOD and GC/28 days; **undecane, CASRN 1120-21-4:** 118% by BOD and 100% by GC/28 days.	**2,2,4-trimethylpentane, CASRN 540-84-1:** Japanese MITI test: 0% by BOD, 3% by GC/28 days; **n-pentane, CASRN 109-66-0:** Japanese MITI test: 96% by BOD and 100% by GC after 28 days.	**methylcyclohexane, CASRN 108-87-2:** 0% by BOD after 28 days; BCF = 181-321 (8wk in Cyprinus caprio @ 10 & 100ppm) **n-heptane, CASRN 142-82-5:** 101% by BOD and 100% by GC after 28 days; **cyclohexane, CASRN 110-82-7:** Japanese MITI test: 0% by BOD, 8% by GC/28days; **toluene, CASRN 108-88-3:** 123% by BOD and 100% by GC/14 days; **n-hexane, CASRN 110-54-3:** 100% by BOD and 100% by GC after 28 days; **2-methylpentane, CASRN 107-83-5:** Japanese MITI test: 93% by BOD, 94% by GC/28 days; **xylene, CASRN 1330-20-7:** OECD 301F: 90%, 94%, and 98% after 28 days; BCF 4.9 - 25.9; **1,3-dimethylbenzene, CASRN**

PMN	P-21-0144	P-21-0145	P-21-0146	P-21-0147
				108-38-3: 39% by O2 consumption, 100% by GC, and 100% by TOC at 14 days; 100% by O2 consumption (BOD) and GC at 28 day; **1,4-dimethylbenzene, CASRN 106-42-3:** 32% and 43% by O2 consumption, 87% and 100% by GC at 28 days; **benzene, CASRN 71-43-2:** 40% by BOD and 69% by GC at 14 days **ethylbenzene, CASRN 100-41-4:** 0% by BOD and HPLC at 28 days.
ECHA data[3]	**m-xylene, CASRN 108-38-3:** OECD 301F: 90-98%/28 days; **1,3,5-trimethyl-benzene, CASRN 108-67-8:** OECD 301F: 61%/28 days; **1-hexene, CASRN 592-41-6:** OECD 301C: 67-98% by BOD, 91-96% by TOC, and 87-94% by GC/28 days; **p-xylene, CASRN 106-42-3:** OECD 301F: 90%/28 days;		**2-methylbutane, CASRN 78-78-4:** OECD 301F: 71.43% after 28 days **n-pentane, CASRN 109-66-0:** OECD 301F: 87%/28 days.	**methylcyclohexane, CASRN 108-87-2:** OECD 301D: 0%/28d (O2 consumption); BCF: 95-321 **110-82-7:** OECD 301F: 77%/28 days; **2-methylpentane, CASRN 107-83-5:** OECD 301C: 93% by BOD, 94% by GC/28 days; **n-octane, CASRN 111-65-9:** >60% after 20 days in equivalent to ready bideg test, BCF = 198.7; **xylene, CASRN 1330-20-7:** 39% by O2 consumption, 100% by GC and TOC @ 14 days; **1,2-dimethylbenzene, CASRN 95-47-6:** OECD 301F: 90%, 94%, and 98% after 28 days; BCF 4.9 - 25.9; **1,3-dimethylbenzene, CASRN 108-38-3:** OECD 301F: 90%, 94%, and 98% after 28 days; BCF 4.9 - 25.9; **1,4-dimethylbenzene, CASRN 106-42-3:** OECD 301F: 90%, 94%, and 98% after 28 days; BCF 4.9 - 25.9; **benzene, CASRN 71-43-2:** OECD 301F: 96% by BOD at 28 days; **ethylbenzene, CASRN 100-41-**

[redacted]

PMN	P-21-0144	P-21-0145	P-21-0146	P-21-0147
				4: OECD 310: 79% at 28 days.
HPV data[4]	**Naphtha (petroleum), light straight-run, CASRN 64741-46-4:** OECD 301F (Mano Resp): 77%/28 days.	**Naphtha (petroleum), light straight-run, CASRN 64741-46-4:** OECD 301F (Mano Resp): 77%/28 days.	**Naphtha (petroleum), light straight-run, CASRN 64741-46-4:** OECD 301F (Mano Resp): 77%/28 days	**Naphtha (petroleum), light straight-run, CASRN 64741-46-4:** OECD 301F (Mano Resp): 77%/28 days
Persistence[5]	**P1-P3 (limited persistence to very persistent)**	**P1-P3 (limited persistence to very persistent)**	**P1-P3 (limited persistence to very persistent)**	**P1-P3 (limited persistence to very persistent)**
Property	Bioaccumulation Potential			
Bioaccumulation factors[6]	29-7,892 (estimated)	29-7,892 (estimated)	29-820 (estimated) **2,2,4-trimethylpentane, CASRN 540-84-1:** BCF: 460-540 (J-Check)	12-1404 (estimated) **methylcyclohexane, CASRN 108-87-2** BCF: 181-321 (J-Check); BCF: 95-321 (ECHA); **n-octane, CASRN 111-65-9:** BCF: 198.7 (ECHA); **xylene, CASRN 1330-20-7:** BCF: 4.9 - 25.9 (J-Check); **1,2-dimethylbenzene, CASRN 95-47-6:** BCF: 4.9 - 25.9 (ECHA); **1,3-dimethylbenzene, CASRN 108-38-3:** BCF: 4.9 - 25.9 (ECHA); **1,4-dimethylbenzene, CASRN 106-42-3:** BCF: 4.9 - 25.9 (ECHA).
Bioaccumulation	**B1-B3 (low to high)**	**B1-B3 (low to high)**	**B1 (low)**	**B1-B2 (low to moderate)**
Comments	[1]US EPA Hazard Characterization 2011. Screening Level Hazard Characterization. Gasoline Blending Streams Category. [2]J -Check/NITE 2021. https://nite.go.jp/chem/jcheck/search.action?request_locale=en [3]ECHA 2021: https://echa.europa.eu/search-for-chemicals [4]HPV 2012. High Production Volume (HPV) Chemical Challenge Program. Gas Oils Category Analysis Document and Hazard Characterization. Submitted to the US EPA by the American Petroleum Institute (API) Petroleum HPV Testing Group. [5]Persistence was evaluated with a weight of evidence approach and included consideration of the BIOWIN model estimations from EPISuite™, the fugacity models for the respective chemical constituents, the measured data for the constituents, and the submitted analogue data. [6]The bioaccumulation potential for the new chemical substances was based on both the bioconcentration (BCF) and bioaccumulation (BAF) model estimations from EPISuite™ and measured data for the constituents.			

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PMN	P-21-0148	P-21-0149	P-21-0150	P-21-0152
Property	Chemical Identity			
Name	[redacted]			
CASRN				
Carbon range				
Data Sources	Analogue Biodegradation Data			
Hazard Characterization[1]	**Naphtha (petroleum), light alkylate, CASRN 64741-66-8**; **Naphtha (petroleum), heavy catalytic reformed, CASRN 64741- 63-5; Naphtha (petroleum), light catalytic cracked, CASRN 64741-55-5**: CONCAWE Inherent (CO2 Headspace) 42-96%/28 days.	**Naphtha (petroleum), light alkylate, CASRN 64741-66-8**; **Naphtha (petroleum), heavy catalytic reformed, CASRN 64741- 63-5; Naphtha (petroleum), light catalytic cracked, CASRN 64741-55-5**: CONCAWE Inherent (CO2 Headspace) 42-96%/28 days.	**Naphtha (petroleum), light alkylate, CASRN 64741-66-8**; **Naphtha (petroleum), heavy catalytic reformed, CASRN 64741- 63-5; Naphtha (petroleum), light catalytic cracked, CASRN 64741-55-5**: CONCAWE Inherent (CO2 Headspace) 42-96%/28 days	No data
J-Check/NITE[2]	**pentane, CASRN 109-66-0:** Japanese MITI Test: 96% by BOD and 100% by GC/28 days; **m-xylene, CASRN 108-38-3:** Japanese MITI test: 30% by O2 consumption, 100% by GC and O2, GC and TOC; **cyclohexane, CASRN 110-82-7:** Japanese MITI test: 0% by BOD, 8% by GC/28days; **1,2-dimethyl-cyclohexane, CASRN 583-57-3:** OECD 301C: 0% by O2 consumption/28 days; **toluene, CASRN 108-88-3:** 123% by BOD and 100% by GC/14 days; **2-methylpentane, CASRN 107-83-5:** Japanese MITI test: 93% by BOD, 94% by GC/28 days; **ethylbenzene, CASRN 100-41-4:** Japanese MITI test: 0% by BOD, 0% by	**undecane, CASRN 1120-21-4:** Japanese MITI Test: 118% by BOD and 100% by GC/28 days; **methylcyclohexane, CASRN 108-87-2:** Japanese MITI Test: 0% by BOD/28 days; **dimethylcyclohexane, CASRN 583-57-3:** OECD 301C 0% by O2 consumption and 2% by GC/28 days; **decahydronaphthalene, CASRN 91-17-8:** Japanese MITI test: 2% by BOD, 3% by GC and 5% by GC/28 days; **trimethylbenzene, CASRN 108-67-8:** 0% by BOD, 0% by GC/14 days; **1,2,4-trimethylbenzene, CASRN 95-63-6:** 9% by BOD and 0% by GC/28 days; **m-xylene, CASRN 108-38-3:** Japanese MITI test: 30% by O2 consumption, 100% by	**pentane, CASRN 109-66-0:** Japanese MITI Test: 96% by BOD and 100% by GC/28 days; **methylcyclohexane, CASRN 108-87-2**: Japanese MITI Test: 0% by BOD/28 days; **toluene, CASRN 108-88-3**: Japanese MITI Test: 123% by BOD and 100% by GC/28 days; **2-methylpentane, CASRN 107-83-5:** Japanese MITI Test: 93% by BOD, 94% by GC/28 days; **hexane, CASRN 110-54-3:** Japanese MITI Test: 100% by BOD and 100% by GC/28 days; **heptane, CASRN 142-82-5:** Japanese MITI Test: 101% by BOD and 100% by GC/28 days; **benzene, CASRN 71-43-2:** Japanese MITI test: 40% by BOD and 69% by GC/14 days;	No data

[redacted]

PMN	P-21-0148	P-21-0149	P-21-0150	P-21-0152
	HPLC	GC and O2, GC and TOC/28 days; **ethylbenzene, CASRN 100-41-1:** 0% by BOD and HPLC/ 28 days; **toluene, CASRN 108-88-3:** 123% by BOD and 100% by GC/28 days; **naphthalene, CASRN 91-20-3:** Japanese MITI test: 2% by BOD and 0% by GC/28 days		
ECHA data[3]	**pentane, CASRN 109-66-0:** OECD 301F: 87%/28 days; **m-xylene, CASRN 108-38-3:** OECD 301F: 90-98%/28 days; **cyclohexane, CASRN 110-82-7:** OECD 301F: 77%/28 days; **2-methylpentane, CASRN 107-83-5:** OECD 301C: 93% by BOD, 94% by GC/28 days; **4-methyl-1-pentene, CASRN 691-37-2:** OECD 301C: 0-3% by BOD and GC after 28 days; **2-methylbutane, CASRN 78-78-4:** OECD 301F: 71.43%/28 days; **p-xylene, CASRN 106-42-3:** OECD 301F: 90%/28 days; **pentene, CASRN 25377-72-4:** OECD 301D: 3-10%/28 days; **2-methyl-2-butene, CASRN 513-35-9:** OECD 301F: 7%/28 days; **ethylbenzene, CASRN 100-41-4:** OECD 310: 70-80% by BOD/28 days	**methylcyclohexane, CASRN 108-87-2**: 0% by BOD after 28 days; **trimethylbenzene, CASRN 108-67-8:** OECD 301F: 61% after 28 days; **p-xylene, CASRN 106-42-3:** OECD 301F: 90% after 28 days; **m-xylene, CASRN 108-38-3:** OECD 301F: 90-98%/28 days; **o-xylene, CASRN 95-45-6:** OECD 301F: 90%, 94%, and 98% after 28 days	**pentane, CASRN 109-66-0:** OECD 301F: 87%/28 days; **methylcyclohexane, CASRN 108-88-3:** OECD 301D: 0%/28 days (O2 consumption); **2-methylpentane, CASRN 107-83-5:** OECD 301C: 93% by BOD, 94% by GC/28 days; **2-methylbutane, CASRN 78-78-4:** OECD 301F: 71.43%/28 days; **benzene, CASRN 71-43-2: OECD 301F:** 96% by BOD at 28 days	No data
HPV data[4]	**Naphtha (petroleum), light straight-run, CASRN 64741-46-4:** OECD 301F (Mano Resp): 77%/28 days.	**Naphtha (petroleum), light straight-run, CASRN 64741-46-4:** OECD 301F (Mano Resp): 77%/28 days	**Naphtha (petroleum), light straight-run, CASRN 64741-46-4:** OECD 301F (Mano Resp): 77%/28 days	Submitted data were not used in the assessment: **Gasoline blending streams (C4-12):** OECD 301F: 77%/28 days; **Kerosene (C9-C16):** OECD 301F: 58.6%/28 days;

[redacted]

PMN	P-21-0148	P-21-0149	P-21-0150	P-21-0152
				Gas oils (C9-25): OECD 301F: 60%/28 days; **Lubricating base oils (C15-50):** OECD 301F: 38%/28 days; **Aromatic extracts (C15-54)**: OECD 301D: 0%; Wa**xes and related materials (C20-50):** OECD 301F: 40%/28 days.
Persistence[5]	**P1-P3 (limited persistence to very persistent)**	**P1-P3 (limited persistence to very persistent)**	**P1-P3 (limited persistence to very persistent)**	**P1-P3 (limited persistence to very persistent)**
Property	Bioaccumulation Potential			
Bioaccumulation factors[6]	29 (estimated)-2,200 (measured)	5 (measured)-511,500 (estimated)	12-2,014 (estimated) **methylcyclohexane, CASRN 108-88-3:** BCF: 95-321 (ECHA); **methylcyclohexane, CASRN 108-87-2**: BCF = 181-321 (J-Check);	3.2-417,600 (estimated)
Bioaccumulation	**B1-B2 (low to moderate)**	**B1-B3 (low to high)**	**B1-B2 (low to moderate)**	**B1-B3 (low to high)**
Comments	[1]US EPA Hazard Characterization 2011. Screening Level Hazard Characterization. Gasoline Blending Streams Category. [2]J -Check/NITE 2021. https://nite.go.jp/chem/jcheck/search.action?request_locale=en [3]ECHA 2021: https://echa.europa.eu/search-for-chemicals [4]HPV 2012. High Production Volume (HPV) Chemical Challenge Program. Gas Oils Category Analysis Document and Hazard Characterization. Submitted to the US EPA by the American Petroleum Institute (API) Petroleum HPV Testing Group. [5]Persistence was evaluated with a weight of evidence approach and included consideration of the BIOWIN model estimations from EPISuite™, the fugacity models for the respective chemical constituents, the measured data for the constituents, and the submitted analogue data. [6]The bioaccumulation potential for the new chemical substances was based on both the bioconcentration (BCF) and bioaccumulation (BAF) model estimations from EPISuite™ and measured data for the constituents.			

[redacted]

PMN	P-21-0153	P-21-0154	P-21-0155	P-21-0156
Property	Chemical Identity			
Name	[redacted]			
CASRN				
Carbon range				
Data Sources	Analogue Biodegradation Data			
Hazard Characterization[1]	No data	No data	No data	No data
J-Check/NITE[2]	No data	**squalane, CASRN 111-01-3:** Japanese MITI Test: 36% by BOD and 51% by GC/28 days; **anthracene, CASRN 120-12-7:** Japanese MITI test: 1.9% by BOD, 3.6% by UVVIS and 0.5% by GC/28 days; **phenanthrene, CASRN 85-01-8:** Japanese MITI test: 54% by BOD, 78.9% by GC and 71.9% by UV-VIS/28 days	**pentadecane, CASRN 629-62-9:** Japanese MITI test: 54.8% by GC, 94.5% by BOD **decahydronapthalene, CASRN 91-17-8:** Japanese MITI test: 2% by BOD, 3% by GC and 5% by GC **1-methylnapthalene, CASRN 90-12-0:** Japanese MITI test: 2% by BOD, 0% by HPLC **anthracene, CASRN 120-12-7:** Japanese MITI test: 1.9% by BOD, 3.6% by UVVIS and 0.5% by GC/28 days	**trimethylbenzene, CASRN 108-67-8:** 0% by BOD, 0% by GC after 14 days; **1,2,4-trimethylbenzene, CASRN 95-63-6:** 9% by BOD and 0% by GC after 28 days; **4-tertbutyltoluene, CASRN 98-51-1:** Japanese MITI test: 52% by BOD, 80% by GC/28 days; **undecane, CASRN 1120-21-4:** 118% by BOD and 100% by GC/28 days; **naphthalene, CASRN 91-20-3:** Japanese MITI test: 2% by BOD and 0% by GC/28 days; **1-methylnaphthalene, CASRN 90-12-0:** Japanese MITI test: 2% by BOD, 0% by HPLC (J-Check); **acenaphthylene, CASRN 208-96-8:** 0% by BOD, 3% by GC/28 days; **acenaphthene, CASRN 83-32-9:** 0% by BOD, 3% by GC/28 days; **fluorene, CASRN 86-73-7**: 0% by BOD, 1% by GC/28 days
ECHA data[3]	No data	**squalane, CASRN 111-01-3**: OECD 301B: 64.7%/28 days; **anthracene, CASRN 120-12-7:** OECD 302C: 1.9% by O2 consumption, 3.6% by GC	**decahydronapthalene, CASRN 91-17-8:** OECD 301D (Closed Bottle test): 53%/28 days **anthracene, CASRN 120-12-7:** OECD 302C: 1.9% by O2 consumption, 3.6% by GC	**trimethylbenzene, CASRN 108-67-8:** OECD 301F: 61% after 28 days (ECHA);
HPV data[4]	Submitted data were not used in the assessment:	Submitted data were not used in the	**CASRN 64741-90-8 and diesel fuel samples):** ISO	**CASRN 64741-90-8 and diesel fuel samples):** ISO 14593:

[redacted]

PMN	P-21-0153	P-21-0154	P-21-0155	P-21-0156
	Gasoline blending streams (C4-12): OECD 301F: 77%/28d; **Kerosene (C9-C16):** OECD 301F: 58.6%/28d; **Gas oils (C9-25):** OECD 301F: 60%/28d; **Lubricating base oils (C15-50):** OECD 301F: 38%/28d; **Aromatic extracts (C15-54**): OECD 301D: 0%; Wa**xes and related materials (C20-50):** OECD 301F: 40%/28d.	assessment: **Gasoline blending streams (C4-12):** OECD 301F: 77%/28d; **Kerosene (C9-C16):** OECD 301F: 58.6%/28d; **Gas oils (C9-25):** OECD 301F: 60%/28d; **Lubricating base oils (C15-50):** OECD 301F: 38%/28d; **Aromatic extracts (C15-54**): OECD 301D: 0%; Wa**xes and related materials (C20-50):** OECD 301F: 40%/28d.	14593: 41%/28d; OECD 301F (Mano Resp): 60%/28d, NRB; OECD 301F (Mano Resp): 57.5%/28d; OECD 301B (Mod Sturm): 40%/28d; **CASRN 64741-59-9:** OECD 301F (Mano Resp): 56%/28d; **CASRN 64741-77-1:** OECD 301F (Mano Resp): 64%/28d, NRB.	41%/28d; OECD 301F (Mano Resp): 60%/28d, NRB; OECD 301F (Mano Resp): 57.5%/28d; OECD 301B (Mod Sturm): 40%/28d; **CASRN 64741-59-9:** OECD 301F (Mano Resp): 56%/28d; **CASRN 64741-77-1:** OECD 301F (Mano Resp): 64%/28d, NRB.
Persistence[5]	**P1-P3 (Limited Persistence to Very Persistent)**	**P1-P3 (Limited Persistence to Very Persistent)**	**P1-P3 (Limited Persistence to Very Persistent)**	**P1-P3 (Limited Persistence to Very Persistent)**
Property	Bioaccumulation Potential			
Bioaccumulation factors[6]	3.2-10,990,000 (estimated)	3.2-808,300 (estimated) **anthracene, CASRN 120-12-7**: BCF: 1660 (J-Check)	41 (measured)-29,200 (estimated) **pentadecane, CASRN 629-62-9**: BCF: 41.4 (J-Check); **decahydronapthalene, CASRN 91-17-8**: BCF: 3050 (J-Check); **1-methylnapthalene, CASRN 90-12-0**: BCF: 660 (J-Check); **anthracene, CASRN 120-12-7**: BCF: 1660 (J-Check)	23 (measured)-808,300 (estimated) **trimethylbenzene, CASRN 108-67-8:** BCF = 142-279 (10wk in cyprinus caprio @ 15 & 150ppm) (J-Check); **1,2,4-trimethylbenzene, CASRN 95-63-6:** BCF = 135-275 (8wk in cyprinus caprio @ 0.2 & 0.02 ppm) (J-Check); **naphthalene, CASRN 91-20-3:** BCF = 23-146 (J-Check); **1-methylnaphthalene, CASRN 90-12-0:** BCF = 360-810 (J-Check); **acenaphthylene, CASRN 208-96-8:** BCF = 225-545 (J-Check); **acenaphthene, CASRN 83-32-9:** BCF = 254-1270 (J-Check); **fluorene, CASRN 86-73-7**: 0% by BOD, 1% by GC/28 days; BCF = 219-830 (J-Check)
Bioaccumulation	**B1-B3 (low to high)**	**B1-B3 (low to high)**	**B1-B3 (low to high)**	**B1-B3 (low to high)**

[redacted]

PMN	P-21-0153	P-21-0154	P-21-0155	P-21-0156
Comments	[1]US EPA Hazard Characterization 2011. Screening Level Hazard Characterization. Gasoline Blending Streams Category. [2]J -Check/NITE 2021. https://nite.go.jp/chem/jcheck/search.action?request_locale=en [3]ECHA 2021: https://echa.europa.eu/search-for-chemicals [4]HPV 2012. High Production Volume (HPV) Chemical Challenge Program. Gas Oils Category Analysis Document and Hazard Characterization. Submitted to the US EPA by the American Petroleum Institute (API) Petroleum HPV Testing Group. [5]Persistence was evaluated with a weight of evidence approach and included consideration of the BIOWIN model estimations from EPISuite™, the fugacity models for the respective chemical constituents, the measured data for the constituents, and the submitted analogue data. [6]The bioaccumulation potential for the new chemical substances was based on both the bioconcentration (BCF) and bioaccumulation (BAF) model estimations from EPISuite™ and measured data for the constituents.			

[redacted]

PMN	P-21-0157	P-21-0158	P-21-0160
Property	Chemical Identity		
Name	[redacted]		
CASRN			
Carbon range			
Data Sources	Analogue Biodegradation Data		
Hazard Characterization[1]	No data	No data	No data
J-Check/NITE[2]	**n-pentadecane, CASRN 629-62-9:** Japanese MITI test: 54.8% by BOD, 94.5% by GC/28 days; BCF = 6.8-41.4 (J-Check); **n-henicosane, CASRN 629-94-7:** Japanese MITI test: 89% by BOD, 72% by GC; **4-tertbutyltoluene, CASRN 98-51-1**: Japanese MITI test: 52% by BOD, 80% by GC/28 days; **1-methylnaphthalene, CASRN 90-12-0:** Japanese MITI test: 2% by BOD, 0% by HPLC; **acenaphthylene, CASRN 208-96-8**: 0% by BOD, 3% by GC/28 days; **acenaphthene, CASRN 83-32-9**: 0% by BOD, 3% by GC/28 days; **fluorene, CASRN 86-73-7:** 0% by BOD, 1% by GC/28 days	**undecane, CASRN 1120-21-4:** 118% by BOD and 100% by GC @ 28 days; **1-isopropyl-4-methylcyclohexane, CASRN 99-82-1:** 78% by BOD, 92% by TOC, 85% by GC at 28 days; **decalin, CASRN 91-17-8:** 2% by BOD, 3% by GC, 5% by GC at 28 days; **1,2,4-trimethylbenzene, CASRN 95-63-6:** 9% by BOD and 0% by GC at 14 days; **1,2,5-trimethylbenzene, CASRN 108-67-8:** 0% by BOD and 0% by GC at 14 days; **1,2,3-trimethylbenzene, CASRN 536-73-8:** 0% by BOD and 6% by GC at 14 days; **naphthalene, CASRN 91-20-3:** Japanese MITI test: 2% by BOD and 0% by GC/28 days;	**1-butene, CASRN 106-98-9:** OECD 107 Kow=2.30; 3% by BOD and 3% by GC at 28 days; **propylene, CASRN 115-07-1:** 1% by BOD, 0% by GC at 28 days
ECHA data[3]	**2,6,10-trimethyldodecane, CASRN 3891-98-3:** OECD 301B: 32.4%/28 days (ECHA)	**isopropylhexane, CASRN 696-29-7:** OECD 310: 1% at 28 days; **1-isopropyl-4-methylcyclohexane, CASRN 99-82-1:** 87% (BODIS TEST) at 28 days; **decalin, CASRN 91-17-8:** OECD 301D: 53% at 28 days; 301F: 0% at 28 days; 301C: 1-3% at 28 days; **isopropylbenzene, CASRN 98-82-8:** 70% by O2 consumption at 20 days; **1-methylnaphthalene, CASRN 90-12-0:** Japanese MITI test: 2% by BOD, 0% by HPLC; **biphenyl, CASRN 92-52-4:** 66% by BOD, 84% by GC, and 91% by UV-VIS at 14 days;	**propane, CASRN: 74-98-6:** Non GLP study: 100% at 16 days

[redacted]

PMN	P-21-0157	P-21-0158	P-21-0160
		2,3-dimethylnaphthalene, CASRN 581-40-8: 50% by BOD, 67% by GC at 28 days; **4-methylbiphenyl, CASRN 644-08-6:** 48% by BOD, 91% by GC, and 100% by UV-VIS at 14 days; **4-ethylbiphenyl, CASRN 5707-44-8:** OECD 301C: 50% by BOD, 77% by GC at 28 days.	
HPV data[4]	**CASRN 64741-90-8 and diesel fuel samples):** ISO 14593: 41%/28d; OECD 301F (Mano Resp): 60%/28d, NRB; OECD 301F (Mano Resp): 57.5%/28d; OECD 301B (Mod Sturm): 40%/28d; **CASRN 64741-59-9:** OECD 301F (Mano Resp): 56%/28d; **CASRN 64741-77-1:** OECD 301F (Mano Resp): 64%/28d, NRB.	**CASRN 64741-90-8 and diesel fuel samples):** ISO 14593: 41%/28d; OECD 301F (Mano Resp): 60%/28d, NRB; OECD 301F (Mano Resp): 57.5%/28d; OECD 301B (Mod Sturm): 40%/28d; **CASRN 64741-59-9:** OECD 301F (Mano Resp): 56%/28d; **CASRN 64741-77-1:** OECD 301F (Mano Resp): 64%/28d, NRB.	No data
Persistence[5]	**P1-P3 (limited persistence to very persistent)**	**P1-P3 (limited persistence to very persistent)**	**P1-P3 (limited persistence to very persistent)**
Property	Bioaccumulation Potential		
Bioaccumulation factors[6]	5 (measured)-1,685,000 (estimated) **n-pentadecane, CASRN 629-62-9:** BCF = 6.8-41.4 (J-Check); **n-hexadecane, CASRN 544-76-3**: BCF = 5-47.9 (J-check); **1-methylnaphthalene, CASRN 90-12-0:** BCF = 360-810 (J-Check); **acenaphthylene, CASRN 208-96-8**: BCF = 225-545 (J-Check); **acenaphthene, CASRN 83-32-9**: BCF = 254-1270 (J-Check); **fluorene, CASRN 86-73-7:** BCF = 219-830 (J-Check)	40 – 4,709,000 (estimated) **decalin, CASRN 91-17-8:** 305C: BCF=839-2340 (J-Check); **1,2,4-trimethylbenzene, CASRN 95-63-6:** BCF = 74-275 (J-Check); **1,2,5-trimethylbenzene, CASRN 108-67-8:** BCF = 142-279 (J-Check); **1,2,3-trimethylbenzene, CASRN 536-73-8:** BCF = 163-210 (J-Check); **1,3-diethylbenzene, CASRN 141-93-5:** BCF = 350-483 (J-Check); **1,4-diethylbenzene, CASRN 105-05-5:** BCF = 546-598 (J-Check); **naphthalene, CASRN 91-20-3:** BCF = 23-146 (J-Check); **1-methylnaphthalene, CASRN 90-12-0:** BCF = 360-810 (J-Check); **4-ethylbiphenyl, CASRN 5707-44-8:** OECD 305: BCF = 180-1200 (J-Check); **1,4-diethylbenzene, CASRN 105-05-5:** 305C: BCF = 320-629 (ECHA).	7-61 (estimated)
Bioaccumulation	**B1-B3 (low to high)**	**B1-B3 (low to high)**	**B1 (low)**
Comments	[1]US EPA Hazard Characterization 2011. Screening Level Hazard Characterization. Gasoline Blending Streams Category.		

PMN	P-21-0157	P-21-0158	P-21-0160
	[2]J -Check/NITE 2021. https://nite.go.jp/chem/jcheck/search.action?request_locale=en [3]ECHA 2021: https://echa.europa.eu/search-for-chemicals [redacted] [5]Persistence was evaluated with a weight of evidence approach and included consideration of the BIOWIN model estimations from EPISuite™, the fugacity models for the respective chemical constituents, the measured data for the constituents, and the submitted analogue data. [6]The bioaccumulation potential for the new chemical substances was based on both the bioconcentration (BCF) and bioaccumulation (BAF) model estimations from EPISuite™ and measured data for the constituents.		

PMN	P-21-0161	P-21-0162	P-21-0163
Property	Chemical Identity		
Name	[redacted]		
CASRN			
Carbon range			
Data Sources	Analogue Biodegradation Data		
Hazard Characterization[1]	No data	No data	No data
J-Check/NITE[2]	[redacted] OECD 107 Kow=2.30; 3% by BOD and 3% by GC at 28 days; [redacted] 1% by BOD, 0% by GC at 28 days	[redacted] Japanese MITI test: 93% by BOD, 94% by GC after 28 days; [redacted] 96% by BOD and 100% by GC after 28 days.	[redacted] 96% by BOD and 100% by GC after 28 days.
ECHA data[3]	[redacted] OECD 301F: 71.43% after 28 days [redacted] Non GLP study: 100% at 16 days	[redacted] OECD 301C: 93% by BOD, 94% by GC after 28 days; [redacted] **OECD 301F: 98%** by O2 consumption at 28 days; [redacted] **OECD 301F:** 98% by O2 consumption at 28 days;	[redacted] OECD 301F: 71.43% after 28 days; [redacted] OECD 301F: 87%/28 days; [redacted] Non GLP study: 100% at 16 days.

[redacted]

PMN	P-21-0161	P-21-0162	P-21-0163
		[redacted] OECD 301F: 71.43% after 28 days; [redacted] OECD 301F: 87%/28 days.	
HPV data[4]	No data	No data	No data
Persistence[5]	**P1-P3 (limited persistence to very persistent)**	**P1 (limited persistence)**	**P1 (limited persistence)**
Property	Bioaccumulation Potential		
Bioaccumulation factors[6]	6-61 (estimated)	29-310 (estimated)	17-148 (estimated)
Bioaccumulation	**B1 (low)**	**B1 (low)**	**B1 (low)**
Comments	[redacted] [2]J -Check/NITE 2021. https://nite.go.jp/chem/jcheck/search.action?request_locale=en [3]ECHA 2021: https://echa.europa.eu/search-for-chemicals [redacted] [5]Persistence was evaluated with a weight of evidence approach and included consideration of the BIOWIN model estimations from EPISuite™, the fugacity models for the respective chemical constituents, the measured data for the constituents, and the submitted analogue data. [6]The bioaccumulation potential for the new chemical substances was based on both the bioconcentration (BCF) and bioaccumulation (BAF) model estimations from EPISuite™ and measured data for the constituents.		

[redacted]

Appendix C: Environmental Hazard Data

C.1 New Chemical Substance Data

There were no environmental hazard data submitted with the NCSs.

C.2 Analogous Mixture/Metabolite/Constituent Data

Environmental hazard data were available for four Tier 2 analogous mixtures. The following robust summaries are from:

The U.S. Environmental Protection Agency Hazard Characterization Document: Screening-Level Hazard Characterization of Gasoline Blending Streams Category (December, 2011).

The American Petroleum Institute (API) Petroleum HPV Testing Group: Gas Oils Category Analysis Document and Hazard Characterization (Consortium #1100997) submitted to the EPA (October, 2012).

C.2.1 Naphtha (petroleum), light alkylate (CASRN 64741-66-8). Paraffinic Naphthas

Tier 2 Analogous Mixture

Acute Toxicity to Fish

Fathead minnow (Pimephales promelas) were exposed to CASRN 64741-66-8 as WAFs in sealed test vessels under static renewal conditions for 96 hours. The loading rates were 0, 1.1, 5.2, 9.7, 19 and 74 mg/L and analytical measurements were made on the WAFs for components comprising ~ 68% of the test substance. Mortality was observed at ≥ 9.7 mg/L. Exposures occurred at a pH of 7.8 – 8.2, a dissolved oxygen concentration of 7.7 – 8.6 mg/L and a temperature of 21.2 °C.

96-h LL50 = 8.2 mg/L

96-h LC50 = 0.305 mg/L

Chronic Value: 0.031 mg/L (An acute to chronic ration (ACR) of 10 was applied to the acute fish endpoint.)

Acute Toxicity to Aquatic Invertebrates

Daphnia magna were exposed to CASRN 64741-66-8 as WAFs under static renewal conditions in sealed test vessels for 48 hours. The loading rates were 0, 9, 18, 35, 70 and 140 mg/L and analytical measurements were made on the WAFs for components comprising ~ 68% of the test substance. Treatment-related effects were observed at ≥ 35 mg/L. Exposures occurred at a pH of 8 – 8.2, a dissolved oxygen concentration of 8.0 – 8.5 and a temperature of 19.1 – 21 °C.

48-h EL50 = 32 mg/L

48-h EC50 = 0.556 mg/L

Toxicity to Aquatic Plants

Green algae (Pseudokirchneriella subcapitata) were exposed CASRN 64741-66-8 as WAFs under static conditions in sealed test vessels for 96 hours. The loading rates were 0, 18, 70, 146, 292 and 1157 mg/L and analytical measurements were made on the WAFs for components comprising ~ 68% of the test substance. Mean measured concentrations were 0, 0.11, 0.31, 0.50, 0.61 and 0.61 mg/L. Exposures occurred at a pH of 7.5 and a temperature of 22 – 26 °C. Growth was inhibited at concentrations ≥ 70 mg/L.

[redacted]

96-h EL50 (biomass) = 45 mg/L
96-h EC50 (biomass) = 0.741 mg/L
Chronic Value: 0.185 mg/L (An acute to chronic ration (ACR) of 4 was applied to the acute algal endpoint.)

Chronic Toxicity to Aquatic Invertebrates
Daphnia magna were exposed CASRN 64741-66-8 as WAFs under static renewal conditions in sealed test vessels for 21 days. The loading rates were 0, 0.44, 1.0, 2.6, 6.4, 16 and 40 mg/L and analytical measurements were made on the WAFs for a subset of components of the test substance. Mean measured concentrations were 0.005, 0.010, 0.016, 0.032, 0.084, 0.23 and 0.46 mg/L. Effects on survival and reproduction were observed at 40 and ≥ 6.4 mg/L, respectively. Exposures occurred at a pH of 7.5 – 8.5, a dissolved oxygen concentration of 8.7 – 9.4 mg/L and a temperature of 19 – 21 °C.
21-d EL50 (survival) > 40 mg/L
21-d EC50 (survival) > 0.46 mg/L
21-d NOEL (survival) = 16 mg/L
21-d NOEC (survival) = 0.23 mg/L
21-d EL50 (reproduction) = 10 mg/L
21-d EC50 (reproduction) = 0.14 mg/L
21-d NOEL (reproduction) = 2.6 mg/L
21-d NOEC (reproduction) = 0.032 mg/L
21-d LOEC (reproduction) = 0.084 mg/L
Chronic Value (reproduction) = 0.052 mg/L

C.2.2 Naphtha (petroleum), light catalytic cracked (CASRN 64741-55-5) Olefinic Naphthas

Tier 2 Analogous Mixture

Acute Toxicity to Fish
Fathead minnows (*Pimephales promelas*) were exposed to CASRN 64741-55-5 as WAFs under static renewal conditions in sealed test vessels for 96 hours. The loading rates were 0 (control), 3, 7.4, 15, 37 and 74 mg/L and analytical measurements were made on the WAFs for components comprising ~ 13% of the test substance. Measured concentrations were not provided. Treatment-related mortality was observed at ≥ 37 mg/L. Exposures occurred at a pH of 7.6 – 8.2, a dissolved oxygen concentration of 5.2 – 8.6 mg/L and a temperature of 21.4 – 21.8 °C.
96-h LL_{50} = 46 mg/L
96-h LC_{50} = 4.1 mg/L
Chronic Value: 0.41 mg/L (An acute to chronic ration (ACR) of 10 was applied to the acute fish endpoint.)

Acute Toxicity to Aquatic Invertebrates
Water fleas (*Daphnia magna*) were exposed to CASRN 64741-55-5 as WAFs under static renewal conditions in sealed test vessels for 48 hours. The loading rates were 0 (control), 6.4, 13, 25, 51 and 102 mg/L and analytical measurements were made on the WAFs for components comprising ~ 13% of the test substance. Measured concentrations were not provided.

[redacted]

Treatment-related effects were observed at 25 mg/L. Exposures occurred at a pH of 7.94 – 8.4, a dissolved oxygen concentration of 8.06 and a temperature of 19.1 – 20.2 °C.
48-h EL_{50} = 18 mg/L
48-h EC_{50} = 1.4 mg/L

Toxicity to Aquatic Plants
Green algae (*Pseudokirchneriella subcapitata*) were exposed to CASRN 64741-55-5 as WAFs under static conditions in sealed test vessels for 96 hours. The loading rates were 0 (control), 6.4, 13, 25, 51 and 102 mg/L and analytical measurements were made on the WAFs for components comprising ~ 13% of the test substance. Measured concentrations were not provided. Exposures occurred at an average pH of 7.5 and a temperature of 22 – 26 °C. Inhibition of growth was observed at ≥ 51 mg/L.
96-h EL_{50} (biomass) = 64 mg/L
96-h EC_{50} (biomass) = 4.6 mg/L
Chronic Value: 1.15 mg/L (An acute to chronic ration (ACR) of 4 was applied to the acute algal endpoint.)

Chronic Toxicity to Aquatic Invertebrates
Water fleas (*Daphnia magna*) were exposed to CASRN 64741-55-5 as WAFs under static renewal conditions in sealed test vessels for 21 days. The loading rates were 0 (control), 0.38, 0.99, 2.6, 6.4, 16 and 40 mg/L and analytical measurements were made on the WAFs for a subset of components of the test substance. Mean measured concentrations were 0.004 (control), 0.007, 0.022, 0.11, 0.27, 0.68 and 3.1 mg/L. Effects on survival and reproduction were observed at 3.1 and ≥ 0.27 mg/L, respectively. Exposures occurred at a pH of 7.2 – 8.2, a dissolved oxygen concentration of 8.4 – 9.1 mg/L and a temperature of 19 – 21 °C.
21-d EL_{50} (survival) = 27 mg/L
21-d EC_{50} (survival) = 1.9 mg/L
21-d NOEL (survival) = 16 mg/L
21-d NOEC (survival) = 0.68 mg/L
21-d LOEC (survival) = 3.1 mg/L
21-d EL_{50} (reproduction) = 13 mg/L
21-d EC_{50} (reproduction) = 0.55 mg/L
21-d NOEL (reproduction) = 2.6 mg/L
21-d NOEC (reproduction) = 0.11 mg/L
21-d LOEC (reproduction) = 0.27 mg/L
Chronic Value (reproduction) = 0.17 mg/L

C.2.3 Distillates (petroleum), light catalytic cracked (CASRN 64741-59-9) Gas oil, light catalytic-cracked (CCGO)

Tier 2 Analogous Mixture

Acute Toxicity to Fish
Rainbow trout (*Onchorhynchus mykiss*) were exposed to CASRN 64741-59-9 as WAFs in sealed test vessels under static renewal conditions for 96 hours with 24-hour renewals. The loading rates of the limit test were 0 (control) and 0.30 mg/L. Analytical measurements were made on the WAFs throughout the test period to determine mean measured concentrations. The mean

[redacted]

concentrations in the control and 0.30 mg/L loadings were <0.004 and 0.21 mg/L respectively. No attempt was made to identify and quantify specific hydrocarbon components solubilized in the WAFs. No mortality or adverse effects were reported. Exposures occurred at a pH of 7.0 – 8.3, a dissolved oxygen concentration of 8.7 – 26 mg/L and a temperature of 14.5 – 17 °C. 96-h LL_{50} > 0.30 mg/L

96-h LC_{50} > 0.21 mg/L

Chronic Value: 0.031 mg/L (An acute to chronic ration (ACR) is not applied to NOEC values from acute tests most toxic endpoint of the 81 petroleum refinery streams in the gasoline blending streams category)

Acute Toxicity to Aquatic Invertebrates

Water fleas (*Daphnia magna*) were exposed to CASRN 64741-59-9 as WAFs under static conditions in sealed test vessels for 48 hours. Four replicates, each containing 5 organisms each, were used for each treatment level. The loading rates used in the test were 0 (control), 0.10, 0.26, 0.64, 1.6, and 4.0 mg/L. Analytical measurements were made on the WAFs throughout the test period to determine mean measured concentrations of <0.014 (control), 0.084, 0.22, 0.58, 1.4, and 3.2 mg/L, respectively. No attempt was made to identify and quantify specific hydrocarbon components solubilized in the WAFs. Percent immobilization at 48 hours in the control (<0.014 mg/L), 0.084, 0.22, 0.58, 1.4, and 3.2 mg/L treatments was 0, 0, 0, 75, 100, and 100%, respectively. Exposures occurred at a pH of 7.9 – 8.9, a dissolved oxygen concentration of 7.9 – 8.6 mg/L and a temperature of 19.3 – 20.7 °C. Water hardness was 178 mg/L as $CaCO_3$.

48-h EL_{50} = 0.51 mg/L

48-h EC_{50} = 0.45 mg/L

Toxicity to Aquatic Plants

Green algae (*Pseudokirchneriella subcapitata*) were exposed CASRN 64741-59-9 as WAFs under static conditions in sealed test vessels for 96 hours. Twelve replicates per treatment were assessed with loading rates of 0 (control), 0.10, 0.32, 1.02, 3.28 and 10.5 mg/L. Analytical measurements were made on the WAFs at the beginning of the test period to determine an initial measured concentrations of <0.014 (control), 0.07, 0.27, 0.93, 2.33, and 5.54 mg/L . No attempt was made to identify and quantify specific hydrocarbon components solubilized in the WAFs. Exposures occurred at a temperature of 23.2°C, with 4170-4345 lux continuous illumination, and a pH of 7.6 – 9.2.

96-h EL_{50} (biomass) = 0.31 mg/L

96-h EL_{50} (yield) = 0.31 mg/L

96-h EL_{50} (growth rate) = 0.80 mg/L

96-h EC_{50} (biomass) = 0.22 mg/L

96-h EC_{50} (yield) = 0.25 mg/L

96-h EC_{50} (growth rate) = 0.70 mg/L

Chronic Value: 0.055 mg/L (An acute to chronic ration (ACR) of 4 was applied to the acute algal endpoint.)

Chronic Toxicity to Aquatic Invertebrates

Water fleas (*Daphnia magna*) were exposed to CASRN 64741-59-9 as WAFs under static renewal conditions in sealed test vessels for 21 days. The loading rates were 0 (control), 0.05, 0.10, 0.18,

[redacted]

0.34, and 0.65 mg/L and analytical measurements were made on the WAFs throughout the test period to determine time-weighted average concentrations of measured hydrocarbons. Time-weighted average concentrations were ND (not detected; control), 0.038, 0.075, 0.14, 0.25, and 0.54 mg/L. Percent immobilization in the 0 (control), 0.038, 0.075, 0.14, 0.25, and 0.54 mg/L groups was 0%, 0%, 10%, 10%, 100%, and 100%, respectively. Sublethal effects included observations of small and lethargic daphnids in the 0.25, and 0.54 mg/L groups. Abnormal appearance (off-color, difficulty swimming) was noted for one adult daphnid in the 0.075 mg/L group from Days 16-20; the adult was then immobile on Day 21. Neonate immobilization was observed twice in the 0.14 mg/L group. Statistically significant differences in adult daphnid growth (length) and neonate production for all surviving treatment groups except the 0.038 mg/L group were present when compared to the control. Exposures occurred at a pH of 7.8-8.67, a dissolved oxygen concentration of 6.65-9.63 mg/L, and a temperature of 20.1-21.9 °C.

21-d EL_{50} (survival) = 0.22 mg/L
21-d EC_{50} (survival) = 0.17 mg/L
21-d NOEL (survival) = 0.18 mg/L
21-d NOEC (survival) = 0.14 mg/L
21-d LOEC (survival) = 0.25 mg/L
21-d EL_{50} (reproduction) = 0.24 mg/L
21-d EC_{50} (reproduction) = 0.18 mg/L
21-d NOEL (reproduction) = 0.05 mg/L
21-d NOEC (reproduction) = 0.038 mg/L
21-d LOEC (reproduction) = 0.075 mg/L
21-day NOEL (growth) = 0.05 mg/L
21-day NOEC (growth) = 0.038 mg/L
21-d LOEC (growth) = 0.075 mg/L
Chronic Value (reproduction and growth) = 0.053 mg/L

C.2.4 Distillates (petroleum), light hydro- cracked (CASRN 64741-77-1) Gas oil, light hydro-cracked (HCGO)

Tier 2 Analogous Mixture

Acute Toxicity to Fish

Rainbow trout (*Onchorhynchus mykiss*) were exposed to CASRN 64741-77-1 as WAFs in sealed test vessels under static renewal conditions for 96 hours with 24-hour renewals. The loading rates of the limit test were 0 (control) and 2.6 mg/L. Analytical measurements were made on the WAFs throughout the test period to determine mean measured concentrations. The mean concentrations in the control and 2.6 mg/L loadings were <0.013 and 0.54 mg/L respectively. No attempt was made to identify or quantify specific hydrocarbon components solubilized in the WAFs. No mortality or adverse effects were reported. Exposures occurred at a pH of 7.0 – 8.3, a dissolved oxygen concentration of 8.7 – 23 mg/L and a temperature of 14.4 – 16.3 °C.

96-h LL_{50} > 2.6 mg/L
96-h LC_{50} > 0.54 mg/L
Chronic Value: 0.031 mg/L (An ACR is not applied to NOEC values from acute tests most toxic endpoint of the 81 petroleum refinery streams in the gasoline blending streams category)

[redacted]

Acute Toxicity to Aquatic Invertebrates

Water fleas (*Daphnia magna*) were exposed to CASRN 64741-77-1 as WAFs under static conditions in sealed test vessels for 48 hours. Four replicates, each containing 5 organisms each, were used for each treatment level. The loading rates used in the test were 0 (control), 0.10, 0.26, 0.64, 1.6, 4.0 and 10.0 mg/L. Analytical measurements were made on the WAFs throughout the test period to determine mean measured concentrations of <0.032 (control), 0.040, 0.080, 0.17, 0.37, 0.81, and 1.7 mg/L, respectively. No attempt was made to identify and quantify specific hydrocarbon components solubilized in the WAFs. No attempt was made to identify and quantify specific hydrocarbon components solubilized in the WAFs. Percent immobilization at 48 hours in the <0.032 (control), 0.040, 0.080, 0.17, 0.37, 0.81, and 1.7 mg/L treatments was 0, 0, 5, 10, 30, 30, and 75%, respectively. Other effects include 58% lethargy in the 0.080 mg/L treatment, and 100 % lethargy in all treatments ≥ 0.17 mg/L. Exposures occurred at a pH of 8.0 – 8.6, a dissolved oxygen concentration of 8.1 – 9.0 mg/L and a temperature of 19.4 – 20.8 °C. Water hardness was 178 mg/L as $CaCO_3$.

48-h EL_{50} = 5.5 mg/L

48-h EC_{50} = 1.0 mg/L

Toxicity to Aquatic Plants

Green algae (*Pseudokirchneriella subcapitata*) were exposed CASRN 64741-77-1 as WAFs under static conditions in sealed test vessels for 96 hours. Twelve replicates per treatment were assessed with loading rates of 0 (control), 0.10, 0.32, 1.02, 3.28 and 10.5 mg/L. Analytical measurements were made on the WAFs at the beginning of the test period to determine initial measured concentrations of <0.032 (control), 0.028, 0.087, 0.22, 0.54, and 1.65 mg/L, respectively. No attempt was made to identify and quantify specific hydrocarbon components solubilized in the WAFs. Exposures occurred at a temperature of 23.8°C, with 4231-4427 lux continuous illumination, and a pH of 7.7 – 9.4.

96-h EL_{50} (biomass) = 3.0 mg/L

96-h EL_{50} (yield) = 3.0 mg/L

96-h EL_{50} (growth rate) = 5.3 mg/L

96-h EC_{50} (biomass) = 0.51 mg/L

96-h EC_{50} (yield) = 0.51 mg/L

96-h EC_{50} (growth rate) = 0.85 mg/L

Chronic Value: 0.128 mg/L (An ACR of 4 was applied to the acute algal endpoint.)

Chronic Toxicity to Aquatic Invertebrates

Water fleas (*Daphnia magna*) were exposed to CASRN 64741-77-1 as WAFs under static renewal conditions in sealed test vessels for 21 days. The loading rates were 0 (control), 0.04, 0.08, 0.16, 0.32, and 0.64 mg/L and analytical measurements were made on the WAFs throughout the test period to determine time-weighted average concentrations of measured hydrocarbons. Time-weighted average concentrations were ND (not detected; control), 0.013, 0.021, 0.037, 0.072, and 0.13 mg/L. No immobilization or abnormal appearance was observed in the control or treatment groups throughout the study, with the exception of one adult daphnid in the 0.13 mg/L group which appeared small and/or off-color from Days 3-14 and then was considered normal until test termination. Neonate immobilization was observed once in the 0.021 mg/L group. No aborted eggs were observed in any group during the study. There were no statistically

[redacted]

significant differences on adult daphnid growth (length) and neonate production for all treatment groups when compared to the control. Exposures occurred at a pH of 7.51-8.49, a dissolved oxygen concentration of 6.15-9.47 mg/L and a temperature of 20.7-22.2 °C. This test is not acceptable, and EPA does not support the use of this study. The test concentrations were not high enough to produce similar effects observed in the acute test at similar concentrations.
21-d EL_{50} (survival) = >0.64 mg/L
21-d EC_{50} (survival) = >0.13 mg/L
21-d NOEL (survival) = 0.64 mg/L
21-d NOEC (survival) = 0.13 mg/L
21-d LOEC (survival) = >0.13 mg/L
21-d EL_{50} (reproduction) = >0.64 mg/L
21-d EC_{50} (reproduction) = >0.13 mg/L
21-d NOEL (reproduction) = 0.64 mg/L
21-d NOEC (reproduction) = 0.13 mg/L
21-d LOEC (reproduction) = >0.13 mg/L
21-day NOEL (growth) = 0.64 mg/L
21-day NOEC (growth) = 0.13 mg/L
21-d LOEC (growth) = >0.13 mg/L
Chronic Value = **>0.13 mg/L**, LOEC unavailable for calculation

[redacted]

Appendix D: The Toxic Unit Approach Used in Tier 3 Environmental Hazard Assessments

The guidance EPA has developed to assess multi-chemical mixtures uses a tiered approach with data for the mixture of concern, data for analogous mixtures, and data for individual mixture constituents (EPA 1986 and 2000). The goal of the constituent-level approach is to evaluate the combined effects of the mixture, using the individual effects of each constituent. For chemical mixtures that are toxicologically similar and share a common toxic mode of action (EPA 1999 and 2002), dose addition is recommended by the Agency frameworks. Dose addition is the default approach in situations where each individual constituent may not reach a threshold to produce effects but may be of concern when combined in a mixture with other similar chemicals (EPA 2000). This is because constituents in a mixture may be limited by physical properties (*e.g.,* water solubility or log K_{OW}) and may not reach a level to be acutely toxic alone, but will additively contribute to the toxicity of the mixture (Di Toro and McGrath 2000; Mayer and Reichenberg, 2009). The biological basis for dose addition is the similarity of chemical constituents regarding toxicologic behavior, such as toxic mechanism, mode of action, or endpoint.

When hazard assessments are completed using constituent analysis and dose addition, the general procedure is to scale the doses of the components by their relative potency, then add the scaled doses together to result in the combined response. The Relative Potency Factor (RPF), Toxicity Equivalence Factor (TEF), and Health Index (HI) are three methods that utilize a scaling factor to account for differences in toxicologic potency, but differ in the required knowledge about toxic mechanism, and in the extent over which toxicologic similarity is assumed (EPA 2000 and 2002). Experimental test data is required in both RPF and TEF, and the scaling factors represent the toxicity relative to an index chemical. Mixture exposure is given by the sum of the scaled exposure levels, and effects are predicted relative to the effects of the index chemical. The HI method, which is most often used by the EPA, is more generally applicable and has fewer data requirements. The HI only requires similarity in target tissue (as is the case for baseline narcosis) and is determined for each constituent using scaling factors based on each component's respective toxicity. If the summed HI exceeds unity, the concern is the same as if an individual chemical exceeded its acceptable level by the same proportion.

Fuel-stream mixtures are comprised of hydrocarbons, which are classified as neutral organic chemicals that assert toxicity to environmental organisms via non-polar narcosis. Because hydrocarbons share this common, additive toxic mode of action (narcosis), the toxicity of fuel-stream mixtures is assumed to result from the additive contribution of each constituent (Capuzzo 1987, Di Toro and McGrath 2000, Barata *et al.* 2005, McGrath *et al.* 2005, Redman *et al.* 2012). Fuel-stream mixtures can be evaluated with a hazard index referred to as the Toxic Unit (TU) approach, which characterizes mixture toxicity by combining the toxic contributions of the individual constituents (Di Toro and McGrath 2000), and is the recommended method for comparisons of physically and chemically dispersed oil according to the National Academies of Sciences and Medicine (2020). In the TU approach, each fuel stream constituent (*i*) is assigned a toxic unit (TU_i), which is the ratio between the aqueous concentration of the constituent (C_W), and the corresponding effect concentration (i.e., EC_{50} or LC_{50}) in the same medium (Equation 1).

$$1) \quad TU_i = \frac{C_W}{LC_{50}}$$

[redacted]

The TU approach relies on the assumption that the toxicity of a mixture is equal to the additive toxicity of the individual constituents, so the TU_s for each constituent are summed to result in the total TU for the mixture (TU_{mix}) (Equation 2).

$$2) \quad TU_{mix} = \sum_i TU_i$$

When LC_{50}'s are used in the approach, and the combined TUs (TU_{mix}) for a chemical mixture at a certain concentration are equal to one, then that concentration is equal to the mixture LC_{50} (Di Toro and McGrath 2000, McGrath and Di Toro 2009). The TU approach can be applied to a variety of toxicity endpoints (*e.g.,* acute aquatic invertebrate EC_{50} or chronic values), provided there is consistency between the endpoints being used for each constituent. When the summed TU exceeds unity (=1), the effects of the mixture are equivalent to those observed when a single chemical exceeds its threshold by the same proportion.

Toxic Unit Methodology

The TU approach is often used to predict the toxicity of chemical mixtures with known concentrations in a laboratory setting and has been successfully used to compare toxicities of six gasoline blending streams (McGrath *et al.* 2005). TUs have also been used to assess groundwater contaminated by volatile hydrocarbons (Brack *et al.* 1998), and sediments contaminated with polycyclic aromatic hydrocarbons (Schwartz *et al.* 1995). In the regulatory setting for risk assessments, exposure concentrations are not considered during evaluation of environmental hazard, and the application of TUs to fuel-stream new chemicals therefore utilizes compositional information provided with each submission to determine appropriate constituents. When a detailed list of compositional information is provided, a TU can be directly calculated for each hydrocarbon in the mixture. When only PIONA[11] profiles are provided, the most toxic constituent within each PIONA class is selected as a worst-case scenario for that class (see "Assumptions and Requirements of the TU Approach"). In both situations, the result is a list of constituent hydrocarbons and their corresponding fraction of the fuel-stream mixture.

In order to estimate mixture toxicity using TUs, a linear relationship between the total mixture TUs and the corresponding mixture concentrations is established. Toxic units are calculated for each constituent listed in the mixture using Equation 1. This uses the most sensitive toxicity endpoint (from ECOSAR[12] predictions for fish, aquatic invertebrate, and algae) and the constituent's exposure concentration. To estimate the exposure concentration for each constituent, respective chemical (or PIONA class) fractions are multiplied by an estimated total aqueous concentration[13] (in this case, 1 ppm). The result is an estimated aqueous concentration for each constituent when the total fuel-

[11] PIONA= Hydrocarbon classes: Paraffins, Isoparaffins, Olefins, Naphthenic, and Aromatic

[12] ECOSAR V2.0 QSARs for neutral organics;

[13] The exposure concentrations used are arbitrary, as the goal is to determine the TUs for three concentrations, and perform a linear regression. However, the TUs at 1 ppm are also used to streamline the process, which is described in "Streamlining the TU Approach".

[redacted]

stream concentration is 1 ppm. Using Equations 1 and 2, a TU is calculated for each constituent, and summed to estimate the total TU for the fuel stream at 1 ppm.

The next step to estimate the fuel stream ecotoxicity endpoints (*e.g.,* EC_{50}, LC50, chronic value) is to calculate the TUs for two other selected total mixture concentrations (0.1 and 10 ppm) using the same method. This results in total TU estimates for two additional exposure concentrations, which facilitates the linear regression. An example set of TUs from this approach is listed in Table D-1; using the most sensitive test organism (algae) that was predicted from ECOSAR toxicity endpoints.

Table D-1. The TUs for Individual Constituents within an Example Fuel Stream at Estimated Exposure Concentrations, Calculated Using the Acute Algal Endpoints for Each Chemical

Chemical	PIONA fraction	Algal EC_{50} (ppm)	TUs* at each concentration		
			0.1 ppm	1 ppm	10 ppm
[redacted]		12.405	0.001	0.008	0.081
		13.946	0.003	0.027	0.272
		7.914	0.001	0.008	0.076
		14.882	0.003	0.027**	0.269
		9.639	0.000	0.002	0.021
		-	0.007	0.0718	0.718

*TU= exp conc / EC_{50}
**TU= (0.4 * 1ppm)/ 14.882ppm

In order to estimate the total acute fuel-stream toxicity to the most sensitive species, the exposure concentration that resulted in 1 TU is calculated (TU = 1 at the E/LC_{50}). Using information from multiple exposure concentrations less than 100 mg/L (in this example: 0.1, 1, and 10 ppm, Table 1), a linear regression between the total concentration (C_{mix}) and corresponding mixture TUs can be produced (Equation 3). Equation 4 shows the result of this approach using data from Table 1. Since no exposure results in zero TUs, the *yint* is zero.

3) $TU_{mix} = m * C_{mix} + yint$

4) $TU_{mix} = 0.0718 * C_{mix} + 0$

The aqueous fuel-stream concentration predicted to result in the acute endpoint (algal EC_{50}) was determined by substituting TU = 1, and solving for C_{mix}:

5) $1 = 0.0718 * C_{mix} + 0$

6) $C_{mix} = \frac{1}{0.0718}$

7) $C_{mix} = 13.93 \text{ ppm}$

The estimated acute algal endpoint (the most sensitive species) for this example is 13.93 ppm.

[redacted]

Streamlining the TU Approach

When the total mixture concentration (C_{mix}) is 1 ppm, the total TUs will be equal to the slope of the linear regression in Equation 3:

3) $TU_{mix} = m * C_{mix} + yint$

$TU_{mix} = m * 1 + 0$

$TU_{mix} = m$

The total TUs for a 1 ppm aqueous exposure concentration (0.0718 in Table 1) can be used as the slope of the linear regression (Equation 3), circumventing the need for the calculation of TUs from multiple exposure concentrations:

3) $TU_{mix} = m * C_{mix} + yint$

4) $TU_{mix} = 0.0718 * C_{mix}$

Then, as before, TU_{mix} of 1 is used to solve for C_{mix}, to determine the total mixture concentration resulting in the estimated acute algal endpoint.

5) $1 = 0.0718 * C_{mix}$

6) $C_{mix} = \frac{1}{0.0718}$

7) $C_{mix} = 13.93 \text{ ppm}$

Assumptions and Requirements of the TU Approach

There are inherent assumptions within the TU approach, which have been documented and discussed in great detail (Di Toro and McGrath 2000, Di Toro *et al.* 2000, McGrath *et al.* 2005, McGrath and Di Toro 2009, and Redman *et al.* 2012). Chiefly, this approach assumes individual fuel-stream constituents have a narcotic toxic mode of action, and that this narcosis is additive. Previous guidance on the hazard assessment of mixtures supports these assumptions, and suggests the use of additivity and the hazard index method when data is unavailable and mixtures are composed of chemicals acting via the same toxicological pathway (EPA 1986, 1999, 2000, and 2002). The TU approach is a hazard index that does not require any additional assumptions outside those discussed in these agency guidelines.

The prediction of mixture effects does rely on the linear relationship that has been established between TUs and total aqueous concentration. The linear relationship between TUs and aqueous concentrations is indicative of levels <100 ppm total concentration. There is uncertainty in this linear relationship beyond 100 ppm, but those concentrations are well above the water solubility limit of many fuel streams, which does not impact the use of TUs in this approach.

A principle requirement of the TU approach is the adequate identification of the fuel-stream constituents. In order to assign TUs for each hydrocarbon listed in the fuel stream, a detailed list of hydrocarbon constituents and their fraction of the mixture is needed. Constituent identities are often absent from the limited compositional data provided with submitted fuel-stream NCSs. When only limited compositional data are provided, each PIONA class or subclass (*e.g.,* 1-ring vs 2-ring aromatics) is assigned a representative constituent within the range of physical properties (*e.g.,* log K_{OW} and water

[redacted]

solubility) of the mixture. In order to determine this representative constituent for each class/subclass in the mixture, a database from the Conservation of Clean Air and Water in Europe (CONCAWE) was searched (obtained from Redman et al. 2014). This library consists of 1563 chemical compounds that are known to be present in hydrocarbon mixtures. The CONCAWE database is filtered for the properties of the mixture and the chemical class in question, and the constituent with the highest log K_{OW} below the limits of acute or chronic effects is selected as a worst-case scenario for that class. These representative constituents are input into ECOSAR to obtain ecotoxicity endpoints for each class or subclass.

In ECOSAR, acute effects of *discrete* neutral organic chemicals are limited to chemicals with log K_{OW} < 5.0 (or <6.4 for algae). *In silico* modeling (*i.e.,* ECOSAR) predicts toxicity endpoints based on a single chemical at 100% of the volume, and does not consider that the toxic contribution from each constituent occurs at a concentration far below the physical-chemical limits of the neutral organics ECOSAR chemical class. Additionally, chemicals with higher log K_{OW}'s have been documented to contribute to the toxicity of mixtures (Di Toro and McGrath 2000; Mayer and Reichenberg, 2009). The TU approach will consider acute effects from constituents with log K_{OW} < 7.0 as contributors to additive toxicity, while chronic effects will continue to consider constituents with log K_{OW} < 8.0. After filtering for hydrocarbons within these limits, chemicals with the highest log K_{OW} were selected as representatives for the individual PIONA classes; "no effects at saturation" or "NES" were predicted for classes if all constituents were above the log K_{OW} limits. Although this provided an inherently conservative estimate of mixture toxicity, the worst-case scenario approach is necessary to avoid underestimating effects when the identity of the constituents is unknown.

Lastly, the TU approach requires adequate characterization of the mixture to properly estimate toxicity. If compositional information is missing for much of the mixture, the TUs may be underestimated, and will fail to accurately depict the toxicity endpoints of the mixture. Additionally, if compositional information is lacking for a small fraction of the mixture, but that fraction is the most toxic, TUs will be underestimated. Therefore, when the submitted compositional information inadequately characterizes the fuel stream, TUs will not properly predict toxicity, and estimates should be based on the most toxic constituent listed (Tier 4: Screening Level Assessment). This is consistent with the previous method used in the environmental hazard assessment of fuel-stream NCSs.

Application of Toxic Units

The following steps are taken to assign environmental hazard to chemical mixtures being assessed with Tier 3.

1. Determine the list of constituents and their respective proportion of the mixture using one of two methods.
    a. Direct listing of constituents by submitter
    b. Representative constituents from PIONA profiles and physical properties with conservative assumptions when submission lacks details
2. Predict the ecotoxicity endpoints for each constituent, using ECOSAR's neutral organics chemical class.
3. For each ecotoxicity endpoint, calculate the TU for each constituent
    a. Use a 1 ppm total aqueous concentration

   b. TU = (1 ppm * Constituent proportion) / Specific Endpoint
4. For each ecotoxicity endpoint, sum the total TUs calculated in Step 3 = TU_{mix}
5. Determine the mixture's threshold concentration for each ecotoxicity endpoint
   a. 1 / TU_{mix} = mixture threshold concentration
6. Calculate the COCs for each ecotoxicity endpoint using appropriate assessment factors for neutral organics
   a. Acute fish and acute aquatic invertebrate use AF = 5; acute algae uses AF = 4
   b. Chronic values use AF = 10
7. Select the taxa (*e.g.,* fish, aquatic invertebrate, or algae) with the lowest COCs
   a. Acute and chronic endpoints do not have to come from the same taxa

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[redacted]

Appendix E: Supplementary Information to the Environmental Hazard Assessment

Table E-1. Ecotoxicity Endpoints for the Fuel-Stream NCSs with Detailed Chemical Composition

NCS	Class[A] stream fraction	Chemical name CASRN	Chemical fraction (%)	ECOSAR predicted toxicity endpoints[B] (ppm)					
				Fish 96-h LC_{50}	Aq Invert 48-h EC_{50}	Algae 96-h EC_{50}	Fish ChV[C]	Aq Invert ChV	Algae ChV
P-21-0160	[redacted]			25.37	**14.82**	12.40	2.56	**1.56**	3.46
				29.53	**17.13**	13.95	2.96	**1.77**	3.83
				13.28	**8.06**	7.91	1.40	**0.95**	2.40
				32.47	**18.73**	14.88	3.23	**1.91**	4.04
				17.30	**10.36**	9.64	1.80	**1.17**	2.85
P-21-0161				25.37	**14.82**	12.40	2.56	**1.56**	3.46
				29.53	**17.13**	13.95	2.96	**1.77**	3.83
				13.28	**8.06**	7.91	1.40	**0.95**	2.40
				32.47	**18.73**	14.88	3.23	**1.91**	4.04
P-21-0162				11.41	**6.97**	7.04	1.22	**0.83**	2.17
				25.37	**14.82**	12.40	2.56	**1.56**	3.46
				5.74	**3.65**	4.32	0.64	**0.49**	1.45
				13.28	**8.06**	7.91	1.40	**0.95**	2.40

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

NCS	Class[A] stream fraction	Chemical name CASRN	Chemical fraction (%)	ECOSAR predicted toxicity endpoints[B] (ppm)					
P-21-0163	[redacted]			25.37	**14.82**	12.40	2.56	**1.56**	3.46
				11.41	**6.97**	7.04	1.22	**0.83**	2.17
				29.53	**17.13**	13.95	2.96	**1.77**	3.83
				13.28	**8.06**	7.91	1.40	**0.95**	2.40

[A]Class refers to the PIONA class (P= paraffin, I= isoparaffin, O= olefins, N= naphthenic, A= aromatic); [B]Endpoints estimated using neutral organics chemical class in ECOSAR (V2.0); [C]ChV = chronic value; **BOLD** indicates the endpoints most protective of the environment following application of assessment factors.

Table E-2. Ecotoxicity Endpoints for the Fuel-Stream NCSs that Used the Toxic Unit Approach with Representative Constituents for Each Hydrocarbon Class or Subclass

NCS	Class[A] stream fraction	Subclass[B] stream fraction	Chemical[C] used for acute effects CASRN/SMILES	Acute toxicity endpoints[D] (ppm)			Chemical[C] used for chronic effects CASRN/SMILES	Chronic toxicity endpoints[D] (ppm)		
				Fish 96-h LC_{50}	Invert 48-h EC_{50}	Algae 96-h EC_{50}		Fish ChV	Invert ChV	Algae ChV
P-21-0144	[redacted]			0.350	**0.256**	0.548	n-Tridecane 629-50-5	**0.001**	0.002	0.024
				0.404	**0.294**	0.612	3-Methylundecane 1002-43-3	**0.004**	0.006	0.048
				0.995	**0.692**	1.189	Same-as acute	**0.123**	0.118	0.488
				0.500	**0.360**	0.718	n-Octylcyclopentane 1795-20-6	**0.002**	0.003	0.030
				0.789	**0.561**	1.057	Same-as acute	**0.101**	0.102	0.456
P-21-0152				No toxicity predicted; minimum log K_{ow} > 7			Same-as acute*	No toxicity predicted; minimum log K_{ow} > 8		

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

NCS	Class[A] stream	Subclass[B] stream	Chemical[C] used for acute effects	Acute toxicity endpoints[D] (ppm)			Chemical[C] used for chronic effects CASRN/SMILES	Chronic toxicity endpoints [D] (ppm)		
	[redacted]			0.008	**0.007**	0.034	2-Heptylphenanthrene c1cc2c3ccc(CCCCCCC)cc3ccc2cc1	**0.0002**	0.0006	0.0076
				0.017	**0.015**	0.062	Same-as acute	**0.0027**	0.0046	0.0416
P-21-0153				No toxicity predicted; minimum log K_{ow} > 7			Same-as acute*	No toxicity predicted; minimum log K_{ow} > 8		
				No toxicity contribution; minimum log K_{ow} > 7			1-Methylnonylcyclohexane C1CCCCC1C(C)CCCCCCCC	0.0002	**0.0004**	0.0054
				0.024	**0.020**	0.078	Octamethyldecalin CC1C(C)C(C)C2C(C)C(C)C(C)C(C)C2C1C	0.0004	**0.0008**	0.0100
				0.092	**0.073**	0.219	n-Propyl-hydro-Chrysene C1CCC2CCC3C4CCC(CCC)CC4CCC3C2C1	0.0004	**0.0008**	0.0104
				0.016	**0.014**	0.057	n-Dodecylbenzene 123-01-3	0.0002	**0.0004**	0.0060
P-21-0154				No toxicity predicted; minimum log K_{ow} > 7			Same-as acute	No toxicity predicted; minimum log K_{ow} > 8		
				0.017	**0.015**	0.058	1-Methylnonylcyclohexane C1CCCCC1C(C)CCCCCCCC	**0.0002**	0.0004	0.0054
				0.118	**0.092**	0.256	2,4 dimethylhexyl-2-decalin C1CCC2CCC(CC(C)CC(C)CC)CC2C1	**0.0002**	0.0004	0.0063
				0.203	**0.155**	0.395	n-Pentyl-hydro-Phenanthrene C1CCC2CCC3CC(CCCCC)CCC3C2C1	**0.0004**	0.0008	0.0100
				0.032	**0.026**	0.099	n-Propyl-hydro-Chrysene C1CCC2CCC3C4CCC(CCC)CC4CCC3C2C1	**0.0004**	0.0008	0.0104

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

NCS	Class[A] stream	Subclass[B] stream	Chemical[C] used for acute effects	Acute toxicity endpoints[D] (ppm)			Chemical[C] used for chronic effects CASRN/SMILES	Chronic toxicity endpoints[D] (ppm)		
	[redacted]			0.106	**0.083**	0.235	n-Dodecylbenzene 123-01-3	**0.0002**	0.0004	0.0059
				0.4188	**0.3083**	0.6713	4-octylbiphenyl c1ccccc1c2ccc(CCCCCCCC)cc2	**0.0003**	0.0006	0.0084
				1.1500	**0.8090**	1.4700	2-Heptylphenanthrene c1cc2c3ccc(CCCCCCC)cc3ccc2cc1	**0.0002**	0.0006	0.0076
				0.3882	**0.2889**	0.6586	Dimethylpyrene c1cc3cc(cc4ccc2c(c1ccc2C)c34)C	**0.0069**	0.0100	0.0780
P-21-0157				0.0013	**0.0012**	0.0082	2,2,4,4,5,5,7,7-Octamethyloctane 5171-85-7	**0.0002**	0.0005	0.0070
				0.0810	**0.0640**	0.1850	n-Octylcyclohexane 1795-15-9	**0.0008**	0.0016	0.0166
				0.5618	**0.4061**	0.8206	Octamethyldecalin CC1C(C)C(C)C2C(C)C(C)C(C)C(C)C2C1C	**0.0004**	0.0008	0.0105
				0.2040	**0.1560**	0.3960	n-Pentyl-hydro-Phenanthrene C1CCC2CCC3CC(CCCCC)CCC3C2C1	**0.0004**	0.0008	0.0100
				0.4308	**0.3147**	0.6646	n-Dodecylbenzene 123-01-3	**0.0002**	0.0004	0.0059
				0.4181	**0.3077**	0.6703	1-Nonylnaphthalene 26438-26-6	**0.0003**	0.0007	0.0091

[A]Class refers to the PIONA class (P= paraffin, I= isoparaffin, O= olefins, N= naphthenic, A= aromatic);
[B]The highest resolution constituent information listed in the chemistry report;
[C]The representative chemical with the highest toxicity in each subclass;
[D] Endpoints estimated using neutral organics chemical class in ECOSAR (V2.0);
[E]1,4 dimethylindane was used to represent the 60% aromatics, because it was the most toxic aromatic listed (only 23/60% of aromatics were listed, with none listed above 9%);
ChV = chronic value;
BOLD indicates the endpoints most protective of the environment following application of assessment factors;
*= no effects are predicted because all chemicals within the properties of the NCS and subclass have logKows above the limit for acute (7) or chronic (8) effects

[P-21-0144 through 0150, P-21-0152 through 0158, and P-21-0160 through 0163]

[redacted]

Table E-3. Ecotoxicity Endpoints Estimated for Each Fuel-Stream Mixture from Analogous Fuel-Streams (Tier 2) or the Toxic Unit approach (Tier 3)

NCS	Tier	Acute			Chronic		
		Fish 96-h LC_{50}	Invert 48-h EC_{50}	Algae 96-h EC_{50}	Fish ChV	Invert ChV	Algae ChV
P-21-0144	3	0.617	**0.443**	0.868	**0.007**	0.011	0.092
P-21-0145	2	**0.305**	0.556	0.741	**0.031**	0.052	0.185
P-21-0146	2	**0.305**	0.556	0.741	**0.031**	0.052	0.185
P-21-0147	2	4.1	**1.4**	4.6	0.41	**0.17**	1.15
P-21-0148	2	4.1	**1.4**	4.6	0.41	**0.17**	1.15
P-21-0149	2	**0.305**	0.556	0.741	**0.031**	0.052	0.185
P-21-0150	2	4.1	**1.4**	4.6	0.41	**0.17**	1.15
P-21-0152	3	0.011	**0.010**	0.047	**0.0004**	0.001	0.013
P-21-0153	3	0.118	**0.099**	0.387	**0.0004**	0.001	0.013
P-21-0154	3	0.056	**0.047**	0.169	**0.0003**	0.001	0.008
P-21-0155	2	>0.21	0.45	**0.22**	**0.031**	0.053	0.055
P-21-0156	2	>0.21	0.45	**0.22**	**0.031**	0.053	0.055
P-21-0157	3	0.253	**0.195**	0.510	**0.0003**	0.001	0.009
P-21-0158	2	>0.54	1	**0.51**	**0.031**	>0.13	0.128
P-21-0160	3	28.73	**16.76***	13.92	2.90	**1.76**	3.86
P-21-0161	3	28.69	**16.76***	14.01	2.90	**1.77**	3.90
P-21-0162	3	10.20	**6.324**	6.748	1.11	**0.79**	2.13
P-21-0163	3	23.85	**14.06***	12.18	2.44	**1.52**	3.45

*Resulted in a lower COC than algae, due to application of assessment factors;
BOLD indicates the endpoints that were used in the hazard assessment

[redacted]

Appendix F: Human Health Hazard Data

F.1 New Chemical Substance Data

There was no human health hazard information submitted with the NCSs.

F.2 Analogous Mixture/Metabolite/Constituent Data

For many of the dose/concentration values reported in the summaries, an "adjusted value" is also reported. These values were used to compare PODs. Only robust summaries for the analogous mixtures/constituents used as PODs or used to identify hazards are provided here; other information is identified with citations.

F.2.1 Naphtha (petroleum), heavy straight-run, CASRN 64741-41-9

Structure not available

Tier 2 Analogous Mixture

ChemView Database:

- Test Guideline Not Specified: Combined Repeated Dose with Repro/Dev Toxicity Screening in rats. Sprague-Dawley rats (12/sex/group) were exposed to the test substance as a vapor via whole body exposure at measured concentrations of 0, 0.46, 2.37 or 13.4 mg/L for 30-54 days (14 days prior to mating, up to 14 days during mating, and during gestation up to GD 19) for 6 hrs/day. Pups were observed until LD4. No effects on the following: parental mortality, clinical chemistry, hematology, or neurobehavioral parameters, number of corpora lutea, implantation sites, post-implantation losses, number of pups born, love born index, viability index, sex ratio, clinical observations of pups, pup body weight or body weight gain.
  - In all doses, hyaline droplet accumulation in males.
  - At 2.37 mg/L: increased kidney weights (unsp.) in males.
  - At 13.4 mg/L: stained, wet fur, significant decreased in body weight, weight gain, and food intake in females, increased liver weights and hepatocellular hypertrophy, increased kidney weights (unsp.) in females, minimal hypertrophy of thyroid follicular epithelium.
  - Parental systemic NOAEL = 2.37 mg/L and LOAEC = 13.4 mg/L based on signs of liver toxicity and minimal hypertrophy of thyroid follicular epithelium. Maternal NOAEC = 2.37 mg/L (593 mg/m^3 adjusted for continuous exposure) and LOAEC = 13.4 mg/L based on reduced body weight, body weight gain and food consumption and minimal hypertrophy of thyroid follicular epithelium. Developmental and Repro NOAEC = 13.4 mg/L based on no effects observed at the highest dose tested.

F.2.2 Naphtha (petroleum), heavy catalytic cracked, CASRN 64741-54-4

No structure available

Tier 2 Analogous Mixture

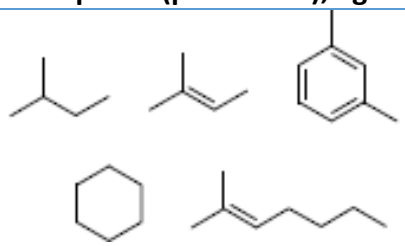
[redacted]

ECHA Database:

- Test Guideline Not Specified: 28-day oral toxicity study in male Fischer 344 rats via gavage. Four naphtha streams (light catalytic cracked naphtha, CASRN 64741-55-5; light catalytic reformed naphtha, CASRN 64741-63-5; heavy catalytic cracked naphtha, CASRN 64741-54-4; and light alkylate naphtha, CASRN 64741-66-8) and fifteen pure hydrocarbons were tested at doses of 500 or 2000 mg/kg/day for 5 days/week for 4 weeks. The concurrent negative control group was administered saline at 2000 mg/kg/day and a concurrent positive control group was administered an unleaded gasoline sample at 500 or 2000 mg/kg/day. Naphtha treatments were administered neat (no vehicle). Rats were observed twice daily for mortality and clinical signs and all animals found dead or moribund were subjected to gross necropsy. Body weights were assessed only prior to dosing on Day 1 and at scheduled sacrifice. At the conclusion of the exposure period, kidneys were weighed and fixed and histopathological examinations were limited to grading severity of three specific kidney histopathological observations: (1) foci of regenerative epithelium in the renal cortex; (2) foci of intratubular cast formation located between the inner and outer stripe of the renal medulla; and (3) hyaline droplet accumulation within the epithelial cells of the proximal convoluted tubules. The severity scores of these three kidney observations were manipulated to produce a "nephropathy score" for each individual animal. All tissues other than the kidney were discarded after gross necropsy and not assessed for histopathology. It was reported that lethargy was the primary clinical sign of toxicity in this study. Portal-of-entry effects of the stomach (including erythema, erosion of the gastric mucosa, raised discolored foci on the gastric epithelial lining, and ulceration) were observed upon gross necropsy and appeared to be generally dose-related. Kidney and liver lesions observed upon gross necropsy included discoloration and mottling, which were postulated by the study authors to be due to post-mortem changes, as the changes were mainly observed in animals with unscheduled deaths. The observations of lethargy and stomach, kidney, and liver gross necropsy findings were reported as summarized findings for the entire study; it was not reported which test substances and at which doses these findings were observed. It is not possible to determine which test substances at which doses resulted in lethargy and the stomach, kidney, and liver gross necropsy findings based on the data provided. For animals treated with heavy catalytic cracked naphtha, no mortality occurred in either group, body weights were significantly decreased relative to control at ≥ 500 mg/kg/day, nephropathy scores were significantly increased at ≥ 500 mg/kg/day, and kidney weights were not affected in either group. The kidney histopathological findings were stated by the study authors to be indicative of alpha-2u-nephropathy and therefore specific to male rats and not relevant to humans. For heavy catalytic cracked naphtha (CASRN 64741-54-4), a LOAEL of 500 mg/kg/day was established based on decreased body weights; a NOAEL was not established.

[redacted]

F.2.3 Naphtha (petroleum), light catalytic cracked, CASRN 64741-55-5



Tier 2 Analogous Mixture

8(e) Database:

- Test Guideline Not Specified (Acute inhalation toxicity): no deaths at 19.8 mg/L; ataxia, extension of hindlimbs during walking

EPA Hazard Characterization, Gasoline Blending Streams, 2011
Data for Naphtha (petroleum), light catalytic cracked (CASRN 64741-55-5)

Acute Toxicity:

- Paraffins: 30.6% (v/v), Olefins: 45.6%, Naphthenes: 10.4%, Aromatics: 13.1%
  Test Guideline Not Specified: Acute oral toxicity: Sprague-Dawley rats (5/sex/dose) were administered naphtha (petroleum), light catalytic cracked (API 83-20) via gavage at 5000 mg/kg-bw and observed for 14 days following dosing. No mortalities occurred. LD50 > 5000 mg/kg
- Paraffins: 30.6% (v/v), Olefins: 45.6%, Naphthenes: 10.4%, Aromatics: 13.1%
  Test Guideline Not Specified: Acute dermal toxicity: New Zealand White rabbits (4/sex/dose) were administered naphtha (petroleum), light catalytic cracked (API 83-20) via the dermal route at 2000 or 3000 mg/kg-bw under occluded conditions for 24 hours and observed for 14 days following dosing. Mortality occurred in one male and one female in the 2000 mg/kg-bw dose level, but no mortalities occurred in the 3000 mg/kg-bw dose level. LD50 > 3000 mg/kg
- Paraffins: 30.6% (v/v), Olefins: 45.6%, Naphthenes: 10.4%, Aromatics: 13.1%
  Test Guideline Not Specified: Acute inhalation toxicity: Sprague-Dawley rats (5/sex/dose) were exposed whole-body to naphtha (petroleum), light catalytic cracked (API 83-20) at a nominal concentration of 5 mg/L for 4 hours and observed for 14 days following exposure. The mean measured concentration was 5.3 mg/L. No mortalities occurred. LC50 > 5.3 mg/L

Repeated-Dose Toxicity:

- Paraffins: 43.6% (w/w), Olefins: 22.7%, Naphthenes: 9.7%, Aromatics: 24.0%
  Test Guideline Not Specified: Repeated dose toxicity: Sprague-Dawley rats (15/sex/dose) were administered naphtha (petroleum), light catalytic cracked (MEHSL CRU #84152) via the dermal route at 0, 30, 125 or 300 mg/kg-bw/day under open conditions, 5 days/week for 90 days. There were no treatment-related effects on mortality, body weight, hematologic parameters or any indication of systemic toxicity at any dose level. No organs were directly affected as determined by serum chemistry, clinical

observations, organ weights, gross necropsy or microscopic evaluation of organ structures. There were no differences seen in sperm morphology. Moderate erythema and slight edema was observed in males at all dose groups. Histopathological examination revealed mild to moderate epidermal hyperplasia, mild inflammation of the superficial dermis and ulceration in all dose groups. NOAEL = 300 mg/kg-bw/day (based on no systemic effects observed at the highest dose tested)

- Paraffins: 37.7% (v/v), Olefins: 53.7%, Naphthenes: 4.3%, Aromatics: 4.4%
  Test Guideline Not Specified: Repeated dose toxicity: Sprague-Dawley rats (16/sex/dose) were exposed whole-body to a distillate of naphtha (petroleum), light catalytic cracked distillate (LCCN-D) as a vapor at nominal concentrations of 0, 2.3, 7.7 and 23.4 mg/L, 6 hours/day, 5 days/week for 15 weeks and observed for 4 weeks after the exposure ended. Mean measured concentrations were within 0.8% of nominal concentrations. Endpoints included clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, histopathology, neurobehavior and ophthalmoscopy. Body weight gain was lower in females at 23.4 mg/L. During the recovery period, the high-dose males and females exhibited greater food consumption than controls. Decreases in hematocrit and hemoglobin concentration were observed in males at 23.4 mg/L. Reductions in mean corpuscular hemoglobin concentration were observed in males at 7.7 mg/L and in females at 23.4 mg/L. Increases were observed in absolute kidney weight (males only), relative kidney weight (females only) and relative liver weight (both sexes) at 23.4 mg/L. Elevated relative kidney weights were observed in males at ≥ 7.7 mg/L. A dose-related increase in nasal mucosa hyperplasia, indicative of exposure to a mild irritant, was observed (dose spread not reported). An increase in hyaline droplet accumulation was observed in treated males at all doses (protein measurement unspecified but assumed). [14] Renal inflammation and tubular dilatation were observed in males at ≥ 7.7 mg/L. No other treatment-related effects were observed.
  LOAEC (males) = 7.7 mg/L/day (increases in relative kidney weight, renal inflammation and tubular dilatation); NOAEC (males) = 2.3 mg/L/day
  LOAEC (females) = 23.4 mg/L/day (based on reductions in mean corpuscular hemoglobin concentration); NOAEC (females) = 7.7 mg/L/day
- Paraffins: 33.2% (v/v), Olefins: 40.0%, Naphthenes: 10.1%,Aromatics: 16.8%
  Test Guideline Not Specified: Repeated dose toxicity: CD-1 mice (10/sex/dose) were exposed whole-body to naphtha (petroleum), light catalytic cracked (LCCN) as a vapor at nominal concentrations of 0, 0.5, 2 and 8 mg/L, 6 hours/day, 5 days/week for 13 weeks.

[14] This is the text from footnote #9 from the Hazard Characterization (HC): "The presence of nephropathy in association with the hyaline droplet accumulation in male rats suggests that the nephropathy in the males may be occurring by an alpha2u-globulin-mediated mechanism, which appears to be unique to male rats and the response is probably not relevant to humans for purposes of risk assessment. EPA's Risk Assessment Forum has outlined the key events and the data that are necessary to demonstrate this mode of action (Alpha2u-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Rat, EPA/625/3-91/019F"]. One of the key events, alpha2u-globulin accumulation, has not been demonstrated. Therefore, the nephropathy is assumed to be relevant to human health and it is concluded that a NOAEL for nephropathy in male rats was not established."

[redacted]

Mean measured concentrations were 0, 0.53, 2.06 and 7.69 mg/L. Endpoints included clinical signs, body weight, hematology, clinical chemistry, organ weights and histopathology. No treatment-related effects were observed.
NOAEC = 7.69 mg/L/day (based on no effects observed at the highest concentration tested)

- Paraffins: 33.2% (v/v), Olefins: 40.0%, Naphthenes: 10.1%, Aromatics: 16.8%
  Test Guideline Not Specified: Repeated dose toxicity: Sprague-Dawley rats (10/sex/dose) were exposed whole-body to naphtha (petroleum), light catalytic cracked (LCCN) as a vapor at nominal concentrations of 0.5, 2 and 8 mg/L, 6 hours/day, 5 days/week for 13 weeks. Sham controls were included, but no specific details regarding the sham controls were located in the robust summary for this study. Mean measured concentrations were 0.53, 2.06 and 7.69 mg/L. Endpoints included clinical signs, body weight, hematology, clinical chemistry, organ weights and histopathology. Lesions on the skin in the scrotal area were observed in four male rats in the high-dose group. Uterine weights were less than untreated controls at all exposure levels, but not less than the sham controls, and the difference was not dose-related. The number of sperm per gram of cauda epididymis was lower at 7.69 mg/L, compared to the sham controls, but not the untreated controls. No other effects were observed. The decreases in sperm number compared to sham controls were not considered to be treatment-related given the lack of effects on sperm number compared with untreated concurrent controls.
  NOAEC = 7.69 mg/L/day (based on no effects at the highest concentration tested)
- Paraffins: 42.8% (v/v), Olefins: 36.5%, Naphthenes: 10.2%, Aromatics: 10.2%
  Test Guideline Not Specified: Repeated dose toxicity: Sprague-Dawley rats (20/sex/dose) were exposed whole-body to naphtha (petroleum), light catalytic cracked (API 81-03) as a vapor at 0, 5.5, 9.5 and 16.4 mg/L, 6 hours/day, 5 days/week for 13 weeks. Endpoints included clinical signs, body weight, hematology, clinical chemistry, urinalysis, organ weights and histopathology. No mortalities were observed. Exposure-related redness with “red material” around the nose was observed at 16.4 mg/L. Body weights of males at 16.4 mg/L were lower than those of controls. Increased kidney weights (relative or absolute unspecified) were observed in treated males at all dose levels (dose-response not indicated), accompanied by histopathological changes in the renal tubules consistent with light hydrocarbon-induced nephropathy (male-rat specific). Liver weights (relative or absolute unspecified) were increased in males at ≥ 9.5 mg/L and in females at 16.4 mg/L, accompanied by centrilobular hepatocellular hypertrophy, which was compatible with non-specific hepatic enzyme induction.
  LOAEC (males) = 9.5 mg/L/day (based on increased liver weights and centrilobular hepatocellular hypertrophy); NOAEC (males) = 5.5 mg/L/day
  LOAEC (females) = 16.4 mg/L/day (based on increased liver weights and centrilobular hepatocellular hypertrophy); NOAEC (females) = 9.5 mg/L/day

<u>Reproductive Toxicity</u>:

- Paraffins: 37.7% (v/v), Olefins: 53.7%, Naphthenes: 4.3%, Aromatics: 4.4%

[redacted]

Test Guideline Not Specified: Repeated-dose/Reproductive/Developmental toxicity: In a combined reproductive/developmental toxicity screening test, Sprague-Dawley rats (10/sex/dose) were exposed whole-body to a distillate of naphtha (petroleum), light catalytic cracked (LCCN-D) at nominal concentrations of 0, 750, 2500 or 7500 ppm (~ 0, 2.4, 7.9 and 23.8 mg/L) as a vapor, 6 hours/day, 7 days/week for 30 – 47 days, starting 14 days prior to mating and extending through gestation day 19. Dams and their litters were sacrificed on postpartum day 4. Mean measured concentrations were 0, 752, 2512 and 7518 ppm (0, 2.4, 8.0 and 23.9 mg/L). No treatment-related mortalities were observed. Red staining of the snout was observed at concentrations ≥ 8.0 mg/L. At 23.9 mg/L, organ weight changes included increases in absolute and relative kidney weights and relative liver weights in males and increases in absolute and relative spleen weights in females. Hyaline droplet formation and dilatation of tubules in the cortico-medullary junction were observed in males at 23.9 mg/L.[15] There were no effects on parental body weight, food consumption, histology (including testes, epididymides and ovaries), fertility index, live birth index, number of litters, numbers of live and dead pups, number of implantation sites, pup viability, sex ratio and pup body weight. NOAEC (reproductive toxicity) ~ 23.9 mg/L/day (based on no effects observed at the highest concentration tested)

- Paraffins: 33.2% (v/v), Olefins: 40.0%, Naphthenes: 10.1%, Aromatics: 16.8%
  Test Guideline Not Specified: Repeated-dose toxicity: In the repeated-dose inhalation study in described previously, Sprague-Dawley rats exposed to naphtha (petroleum), light catalytic cracked (LCCN) as a vapor at a measured concentration of 7.69 mg/L for 13 weeks had a lower number of sperm per gram of cauda epididymis compared to the sham controls, but not the untreated controls.

<u>Developmental Toxicity</u>:

- Paraffins: 37.7% (v/v), Olefins: 53.7%, Naphthenes: 4.3%, Aromatics: 4.4%
  Test Guideline Not Specified: Repeated-dose/Reproductive/Developmental toxicity: In the combined reproductive/developmental inhalation toxicity screening test in Sprague-Dawley rats exposed to a distillate of naphtha (petroleum), light catalytic cracked (LCCN-D) described previously, no effects were observed on live birth index, number of litters, numbers of live and dead pups, number of implantation sites, pup survival, sex ratio, pup body weight and body weight change. No abnormalities were observed in pups. NOAEC (maternal and developmental toxicity) ~ 23.9 mg/L/day (based on no effects observed at the highest concentration tested)
- Paraffins: 33.2% (v/v), Olefins: 40.0%, Naphthenes: 10.1%, Aromatics: 16.8%

[15] This is footnote 17 from the HC: Nephropathy seen in male rats may be occurring by an alpha 2u-globulin-mediated mechanism (which is male rat-specific and not considered relevant to humans). EPA's Risk Assessment Forum has outlined key events and data that are necessary to demonstrate this mode of action (Alpha 2u-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Rat, EPA/625/3-91/019F).

[redacted]

Test Guideline Not Specified: Developmental toxicity: In a prenatal developmental toxicity test, pregnant female Sprague-Dawley rats (15/dose) were exposed to naphtha (petroleum), light catalytic cracked (LCCN) as a vapor at nominal concentrations of 0, 2 or 8 mg/L, 6 hours/day from gestation days 0 – 19. Mean measured concentrations were 0, 2.2 and 7.7 mg/L. There were no treatment-related clinical abnormalities or differences in body weight in the maternal generation. There was an increase in the number of resorptions at 7.7 mg/L compared to controls; however, this did not appear to affect any fertility parameters. There were no treatment-related effects on the number of implantation sites, preimplantation losses, numbers of live and dead fetuses per litter, number of corpora lutea, sex ratio, fetal weight, crown-rump length and incidence of visceral and skeletal abnormalities. NOAEC (maternal toxicity) = 7.7 mg/L/day (based on no effects observed at the hdt); NOAEC (developmental toxicity) = 2.2 mg/L/day; LOAEC (developmental toxicity) = 7.7 mg/L/day (based on an increase in the number of resorptions)

Genotoxicity:

- Paraffins: 30.6% (v/v), Olefins: 45.6%, Naphthenes: 10.4%, Aromatics: 13.1%
  Test Guideline Not Specified: Genotoxicity: Mouse lymphoma cells were exposed to naphtha (petroleum), light catalytic cracked (API 83-20) in ethanol at concentrations of 50 – 800 nL/mL without metabolic activation and 25 – 500 nL/mL with activation. Positive control and negative controls responded appropriately. Cytotoxicity was observed at 175 nL/mL. Naphtha (petroleum), light catalytic cracked (API 83-20) did not cause an increase in mutation frequency. Naphtha (petroleum), light catalytic cracked was not mutagenic in this assay.
- Paraffins: 42.8% (v/v), Olefins: 36.5%, Naphthenes: 10.2%, Aromatics: 10.2%
  Test Guideline Not Specified: Genotoxicity: Mouse lymphoma cells were exposed to naphtha (petroleum), light catalytic cracked (API 81-03) at unspecified concentrations with and without metabolic activation. Naphtha (petroleum), light catalytic cracked (API 81-03) was not mutagenic with or without activation. No other details were provided. Naphtha (petroleum), light catalytic cracked was not mutagenic in this assay.
- Paraffins: 34.6% (v/v), Olefins: 29.2%, Naphthenes: 14.5%, Aromatics: 21.1%
  Test Guideline Not Specified: Genotoxicity: Mouse lymphoma cells were exposed to naphtha (petroleum), light catalytic cracked (API 81-04) at unspecified concentrations with and without metabolic activation. Naphtha (petroleum), light catalytic cracked (API 81-04) was not mutagenic without activation, but the results were equivocal with activation. No other details were provided. Naphtha (petroleum), light catalytic cracked was equivocal for the induction of mutations in this assay.
- Paraffins: 42.8% (v/v), Olefins: 36.5%, Naphthenes: 10.2%, Aromatics: 10.2%
  Test Guideline Not Specified: Genotoxicity: In a sister chromatid exchange assay, CHO cells were exposed to naphtha (petroleum), light catalytic cracked (API 81-03) at concentrations of 0.05 – 0.3 µL/mL without metabolic activation and 0.03 – 0.2 µL/mL with metabolic activation. A small, but significant ($p < 0.05$) increase in the frequency of

[redacted]

sister chromatid exchange was observed at two intermediate dose levels in the presence of metabolic activation. No increase in sister chromatid exchange frequency was observed without activation. Positive and negative controls responded appropriately. Naphtha (petroleum), light catalytic cracked was equivocal for the induction of sister chromatid exchange in this assay.

- Paraffins: 42.8% (v/v), Olefins: 36.5%, Naphthenes: 10.2%, Aromatics: 10.2%
  Test Guideline Not Specified: Genotoxicity: In a sister chromatid exchange assay, B6C3F1 mice (5/sex/dose) were administered naphtha (petroleum), light catalytic cracked (APR 81-03) in corn oil at concentrations of 0, 200, 1200 or 2400 mg/kg-bw via intraperitoneal injection. Positive and negative controls responded appropriately. A statistically significant ($p < 0.05$) increase in the frequency of sister chromatid exchange was observed at all dose levels. Naphtha (petroleum), light catalytic cracked induced sister chromatid exchange in this assay.
- Paraffins: 34.6% (v/v), Olefins: 29.2%,Naphthenes: 14.5%, Aromatics: 21.1%
  Test Guideline Not Specified: Genotoxicity: In a bone marrow chromosomal aberration assay, Sprague-Dawley rats (15/sex/dose) were administered naphtha (petroleum), light catalytic cracked (API 81-04) in corn oil at concentrations of 0, 0.3, 1 or 3 g/kg-bw via intraperitoneal injection and sacrificed up to 48 hours later. Positive and negative controls responded appropriately. There were no treatment-related increases in chromosomal aberrations. Naphtha (petroleum), light catalytic cracked did not induce chromosomal aberrations in this assay.

Skin Irritation:

- Paraffins: 30.6% (v/v), Olefins: 45.6%, Naphthenes: 10.4%, Aromatics: 13.1%
  Test Guideline Not Specified: Skin irritation: Six rabbits (strain and sex not specified) were administered 0.5 mL of naphtha (petroleum), light catalytic cracked (API 83-20) to intact or abraded skin under occluded conditions for 24 hours and observed for 14 days following dosing. Edema and erythema were observed on both intact and abraded skin. The primary dermal irritation score was 3.7. Naphtha (petroleum), light catalytic cracked was moderately irritating to rabbit skin in this study.
- Paraffins: 33.2% (v/v), Olefins: 40.0%, Naphthenes: 10.1%, Aromatics: 16.8%
  Test Guideline Not Specified: Skin irritation: In the prenatal developmental toxicity test in Sprague-Dawley rats described previously, administration of naphtha (petroleum), light catalytic cracked (LCCN) via the dermal route at 0, 30, 125 or 500 mg/kg-bw resulted in slight to moderate dermal irritation, including erythema, edema, scabbing, flaking and eschar. Naphtha (petroleum), light catalytic cracked was moderately irritating to rat skin in this study.

Eye Irritation:

- Paraffins: 30.6% (v/v), Olefins: 45.6%, Naphthenes: 10.4%, Aromatics: 13.1%
  Test Guideline Not Specified: Eye irritation: Rabbits (9/dose; strain and sex not specified) were administered 0.1 mL of naphtha (petroleum), light catalytic cracked (API 83-20) to

one eye; the other eye served as a control. After 20 – 30 seconds, the treated eyes of three rabbits were rinsed with water for 1 minute. Animals were observed for 7 days after treatment. After 1 hour, primary eye irritation scores were 1.0 and 3.3 for unwashed and washed eyes, respectively. An irritation score of zero was recorded at all other times. Naphtha (petroleum), light catalytic cracked was not irritating to rabbit eyes in this study.

Skin Sensitization:

- Paraffins: 30.6% (v/v), Olefins: 45.6%, Naphthenes: 10.4%, Aromatics: 13.1%
  Test Guideline Not Specified: Skin Sensitization: Guinea pigs (10/sex, strain not specified) were administered 0.4 mL of naphtha (petroleum), light catalytic cracked (API 83-20) to shorn skin under occluded conditions for 6 hours once per week for 3 weeks. After a 2-week resting period, a challenge dose of 0.4 mL of 25% test substance in paraffin oil was applied to a previously untreated site, and animals were observed for 48 hours following treatment. No skin reactions were observed following application of the challenge dose. Naphtha (petroleum), light catalytic cracked was not sensitizing to guinea pig skin in this study.

Carcinogenicity:

- Paraffins: 42.8% (v/v),Olefins: 36.5%,Naphthenes: 10.2%, Aromatics: 10.2%
  Test Guideline Not Specified: Carcinogenicity: C3H/HeJ mice (50 males) were administered 0.05 mL of naphtha (petroleum), light catalytic cracked (API 81-03) via the dermal route 2 times/week to clipped skin for 139 weeks. An increased incidence of malignant dermal neoplasms was observed in exposed mice, relative to control mice. Dermal neoplasms included squamous cell carcinomas and fibrosarcomas. The study authors concluded that naphtha (petroleum), light catalytic cracked (API 81-03) was a weak dermal carcinogen. Naphtha (petroleum), light catalytic cracked was carcinogenic to mice in this study.

Neurotoxicity:

- Paraffins: 37.7% (v/v), Olefins: 53.7%, Naphthenes: 4.3%, Aromatics: 4.4%
  Test Guideline Not Specified: Repeated-dose toxicity: In the repeated-dose inhalation study described previously, Sprague-Dawley rats exposed to a distillate of naphtha (petroleum), light catalytic cracked (LCCN-D) as a vapor were subjected to neurobehavioral measurements, including motor activity and functional operational battery tests. No treatment-related effects were observed on neurobehavior. Naphtha (petroleum), light catalytic cracked was not neurotoxic to rats in this study.

Halder et al. 1985:

Repeated-dose Toxicity:

- Test Guideline Not Specified: 28-day oral toxicity study in male Fischer 344 rats via gavage. Four naphtha streams (light catalytic cracked naphtha, CASRN 64741-55-5; light catalytic reformed naphtha, CASRN 64741-63-5; heavy catalytic cracked naphtha, CASRN

[redacted]

64741-54-4; and light alkylate naphtha, CASRN 64741-66-8) and fifteen pure hydrocarbons were tested at doses of 500 or 2000 mg/kg/day for 5 days/week for 4 weeks. The concurrent negative control group was administered saline at 2000 mg/kg/day and a concurrent positive control group was administered an unleaded gasoline sample at 500 or 2000 mg/kg/day. Naphtha treatments were administered neat (no vehicle). Rats were observed twice daily for mortality and clinical signs and all animals found dead or moribund were subjected to gross necropsy. Body weights were assessed only prior to dosing on Day 1 and at scheduled sacrifice. At the conclusion of the exposure period, kidneys were weighed and fixed and histopathological examinations were limited to grading severity of three specific kidney histopathological observations: (1) foci of regenerative epithelium in the renal cortex; (2) foci of intratubular cast formation located between the inner and outer stripe of the renal medulla; and (3) hyaline droplet accumulation within the epithelial cells of the proximal convoluted tubules. The severity scores of these three kidney observations were manipulated to produce a "nephropathy score" for each individual animal. All tissues other than the kidney were discarded after gross necropsy and not assessed for histopathology. It was reported that lethargy was the primary clinical sign of toxicity in this study. Portal-of-entry effects of the stomach (including erythema, erosion of the gastric mucosa, raised discolored foci on the gastric epithelial lining, and ulceration) were observed upon gross necropsy and appeared to be generally dose-related. Kidney and liver lesions observed upon gross necropsy included discoloration and mottling, which were postulated by the study authors to be due to post-mortem changes, as the changes were mainly observed in animals with unscheduled deaths. The observations of lethargy and stomach, kidney, and liver gross necropsy findings were reported as summarized findings for the entire study; it was not reported which test substances and at which doses these findings were observed. It is not possible to determine which test substances at which doses resulted in lethargy and the stomach, kidney, and liver gross necropsy findings based on the data provided. For animals treated with light catalytic cracked naphtha, no mortality occurred in either group, body weights were significantly decreased relative to control at 2000 mg/kg/day, nephropathy scores were significantly increased relative to control at ≥ 500 mg/kg/day, and kidney weights were not affected in either group. The kidney histopathological findings were stated by the study authors to be indicative of alpha-2u-nephropathy and therefore specific to male rats and not relevant to humans. For light catalytic cracked naphtha (CASRN 64741-55-5), a LOEL of 500 mg/kg/day was established based on kidney effects and a NOAEL of 500 mg/kg/day was established based on decreased body weights at 2000 mg/kg/day.

F.2.4 Distillates (petroleum), light catalytic cracked, CASRN 64741-59-9

Structure not available

Tier 2 Analogous Mixture

[redacted]

HPV Chemical Challenge Program: Gas Oils Category Analysis Documents and Hazard Characterization (submitted by the American Petroleum Institute in 2012)

- Developmental toxicity study in rats (test guideline not specified): A light cycle oil [LCO, CAS RN 64741-59-9, Sample # 08281, 49.1% DMSO extractable PAC, 79.8% aromatic hydrocarbons],was applied to the shaved backs of presumed pregnant rats at dose levels of 0, 25, 50, 125, 250 and 500 mg/kg/day from GD0 – 19 (Mobil, 1988b, Study # 50511). At 1000mg/kg day, animals were treated either from GD0-6 or GD6-15 due to severe irritation observed at the onset of treatment. Gestation day 15 was chosen because it is the last day of treatment in standard EPA/FDA teratology studies of that time period. All animals were sacrificed on GD20. In the dams, erythema and flaking of the skin were observed in all gas oil exposed groups. Skin effects were observed in all but the 25 mg/kg group. At doses greater than 25 mg/kg there was a decrease in maternal body weight and body weight gain compared to the controls, with an accompanying reduction in food consumption. There were no treatment-related findings at necropsy. Blood levels of triglycerides were increased in a dose-related manner in the 250, 500 and 1000 mg/kg groups. Fetal body weights were reduced in the 500 and 1000 mg/kg groups, with only the reduction in the 1000 mg/kg group being statistical significant. Resorptions were also increased in the 1000mg/kg GD6-15 group. There were no significant increases in resorptions at 500mg/kg or lower doses and there were similarly no soft tissue variations and malformations, or skeletal malformations in any of the dose groups. As identified by the investigators, maternal LOAEL = 50mg/kg based on decreased body weight, although statistical significance only occurred at the 250 mg/kg/day level and greater; NOAEL = 25mg/kg. Developmental LOAEL = 500mg/kg; NOAEL = 250mg/kg.

ECHA Database:

- Comparable to OECD 401: LD50 (male rat) = 4660 mg/kg-bw; LD50 (female rat) = 3200 mg/kg-bw; hypoactivity; diarrhoea; yellow or brown-stained anal, genital and abdominal areas; hair loss on abdomen; ataxia; red-stained nose and mouth; prostration; lacrimation; hypothermic to touch; and death (ECHA)
- Comparable to OECD 401: LD50 (male rat) = 4290 mg/kg-bw; LD50 (female rat) = 2700 mg/kg-bw; oral discharge, nasal discharge, abnormal respiration and tools, ataxia, and lethargy (ECHA)
- Comparable to OECD 401: LD50 (female rat) < 5000 mg/kg-bw; oral discharge, nasal discharge, ocular discharge, abnormal respiration, tremors, ataxia, lethargy, moribundity, cold to the touch, abnormal stools, stained coat, and/or alopecia (ECHAComparable to OECD 401: LD50 (rat) = 6790 - 7180 mg/kg-bw; hypoactivity, diarrhoea, yellow-stained urogenital/abdominal area, hair loss on anal region/abdomen/hind legs, ataxia, red-stained nose and mouth, prostration, lacrimation, catalepsy, dyspnoea, possible respiratory congestion, hypothermic to touch, inflamed anal region and death (ECHA)

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- Comparable to OECD 403: LC50 (rat) = 4.65 mg/L; coat abnormalities (oily/wetness), crust around nose at 2 to 4 days post-exposure, skin abnormalities (scabs/flaky), hair loss, urine stain on coat, decreased activity/mobility, and eye abnormalities (ECHA)TGNS: LC50 (rat) = 5400 mg/m3; red crusting of eyes (ECHA)
- Comparable to OECD 403: LC50 (rat) > 4.98 mg/L; lethargy, wet coats, ocular discharge (ECHA)
- Comparable to OECD 403: LC50 (rat) > 3.19 mg/L; oral, nasal, and/or ocular discharge, labored breathing, lethargy, alopecia, and stained coat (ECHA)
- Comparable to OECD 402: LD50 (rabbit) > 2000 mg/kg; dermal irritation (ECHA)
- Comparable to OECD 434: LD50 (rabbit) > 2000 mg/kg; abnormal stools, erythema, oedema, eschar, dry skin, whitish-yellow blanching and/or fissuring (ECHA)
- Comparable to OECD 434: LD50 (rabbit) > 2000 mg/kg; abnormal stools (ECHA)
- Comparable to OECD 404: Irritating in rabbits (ECHA)
- Comparable to OECD 405: Not irritating in rabbits (ECHA)
- EPA OTS 798.4500: Not irritating in rabbits (ECHA)
- Comparable to OECD 406: Not sensitizing in guinea pigs (ECHA)
- Comparable to OECD 476: Positive in mouse lymphoma L5178Y cells with activation; negative without activation (ECHA)
- Comparable to OECD 479: Ambiguous in CHO cells with and without activation (ECHA)
- OECD 475: Negative in rats via intraperitoneal route (ECHA)
- Comparable to OECD 475: Negative in rats via intraperitoneal route (ECHA)
- Comparable to OECD 411: Subchronic Dermal Toxicity: 90-Day Study in Rats at Doses of 0, 8, 25, 125, and 500 and 1,250 mg/kg/day. After 2 weeks of exposure rats dosed at 1250mg/kg/day were terminated due to poor growth and appearance. NOAEL (males) = 25 mg/kg-bw/day based on thymus effects. Decreased body weights and thymus, kidney, adrenal, and liver effects were noted at higher doses. (ECHA).
- Comparable to OECD 410: Repeated Dose Dermal Toxicity: 21/28-Day Study in Rabbits at Doses of 0, 250, 500, and 1000 mg/kg. NOAEL = 500 mg/kg-bw/day based on body weight; serum alkaline phosphatase activity was also decreased by approximately 50-60% in animals treated at 2000 mg/kg body weight/day[16] (ECHA).
- Comparable to OECD 410: Repeated Dose Dermal Toxicity: 21/28-Day Study in Rabbits at Doses of 0, 250, 500, and 1000 mg/kg. Systemic NOAEL = 1000 mg/kg-bw/day based on bone marrow granulopoesis and reduced alkaline phosphatase at 2000 mg/kg. LOAEL (dermal irritation) = ca. 250 mg/kg-bw/day based on dermal irritation at all doses (ECHA).

[16] Note that the apparent error in identifying the serum activity decrease at a dose not reported as being used (2000 mg/kg) is present also at the source (ECHA summary). The full study report was not identifiable to check on this (data source listed as a 1985 unnamed study report).

[redacted]

- OECD 411; EPA OPPTS 870.3250; EPA OTS 798.2250: Subchronic Dermal Toxicity: 90-Day Study in Rats at Doses of 0, 100, 450, or 750 mg/kg-bw/day. LOAEL = 100 mg/kg-bw/day based on hematological effects (ECHA).
- Dermal developmental toxicity study in rats at doses of 0, 50, 333, or 1000 mg/kg/day once daily on GDs 0-20. NOEL (maternal toxicity) = 50 mg/kg-bw/day based on increased incidence of vaginal discharge, decreased body weights, body weight changes, food consumption changes. NOEL (developmental toxicity) = 50 mg/kg-bw/day based on decreased pup body weights and decreased pup survival (ECHA).
- OECD 414; EPA OPPTS 870.3700: Dermal prenatal Developmental Toxicity Study in rats at doses of 0, 100, 450, and 750 mg/kg/day. NOAEL (maternal toxicity) = 100 mg/kg/day based on adverse clinical findings, reductions in food consumption and corresponding lower mean body weight gains or losses, and lower thymus weights (absolute and relative to brain weight). NOAEL (developmental toxicity) = 100 mg/kg/day based on increased post-implantation loss with corresponding decreased mean numbers and litter proportions of viable fetuses, as well as lower mean fetal weights and reduced fetal skeletal ossification (ECHA).
- Comparable to OECD 414: Dermal Prenatal Developmental Toxicity Study in Rats at Doses of 0, 25, 50, 125, 250, 500 and 1000 mg/kg from GD 0-19. NOAEL (maternal toxicity) = 25 mg/kg/day based on skin effects, decreased body weight and bw gain. NOAEL (developmental toxicity) = 500 mg/kg/day based on reduced fetal body weights, increased resorptions (ECHA).
- Comparable to OECD 451: Dermal carcinogenicity study in male mice at doses of 0, 28.5%, 50%, or 100% for 104 weeks. Carcinogenic based on tumor formation at 28.5% (ECHA).
- Comparable to OECD 451: Dermal carcinogenicity study in male mice at doses of 0 and 25 uL for lifetime. Weakly carcinogenic in mice (ECHA).
- Comparable to OECD 451: Dermal carcinogenicity study in male mice at doses of 0 and 50 uL for 2 years. Carcinogenic in mice (ECHA).

F.2.5 Syntower bottoms, 64741-62-4

Structure Not Available
Tier 2 Analogous Mixture

ECHA Database:

- Non-Guideline Study, comparable to OECD 401: LD50 (rat) = 4320 (females) - 5270 (males); hypoactivity, ataxia, prostration, diarrhea, hair loss and eye opacity
- Test Guideline Not Specified: TDLo (rat)=7600 mg/kg bw; nasal/ocular discharge, abnormal stools, tremors, stained coat and/or lethargy
- Non-Guideline Study, comparable to EU Method B.1: LD50 (rat) =5230 (males) to 5820 (females); nasal/ocular discharge, abnormal stools, tremors, stained coat and/or lethargy

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- Non-Guideline Study, comparable to EU Method B.1: LD50 (rat)~ 5000 mg/kg bw; nasal discharge, ocular discharge, ataxia, abnormal stools, stained coat and lethargy
- Non-Guideline Study, comparable to EPA OTS 798.1150: LC50 (rat) (4hr) = 4100 mg/m3; labored breathing, nasal discharge and discolored fur
- Non-Guideline Study, comparable to EPA OTS 798.1150: LC50 (rat) (4hr) ≥3600 mg/m3; respiratory distress, brown material on fur
- Non-Guideline Study, comparable to EPA OTS 798.1150: LC50 (rat) (4hr) ≥320 mg/m3
- Non-Guideline Study, comparable to OECD 434: LD50 (rabbit)
  - 2000 mg/kg bw
- Non-Guideline Study, comparable to EU Method B.3: LD50 (rabbit) > 2000 mg/kg bw; erythema and oedema
- Non-Guideline Study, comparable to EU Method B.3: LD50 (rabbit) > 2000 mg/kg bw; labored breathing, tarry stools, nasal discharge and incoordination
- Test Guideline Not Specified: Moderately irritating in rabbits; occluded
- Non-Guideline Study, comparable to EU Method B.4: Moderately irritating in rabbits; occluded
- Non-Guideline Study, comparable to EU Method B.5: Not irritating to rabbit
- Non-Guideline Study, comparable to EU Method B.5: Not irritating to rabbit
- Non-Guideline Study, comparable to EU Method B.6: Not sensitizing in guinea pig
- Non-Guideline Study: API procedure/Buehler Test. Not sensitizing; guinea pigs
- Non-Guideline Study: Buehler Method: Not sensitizing in guinea pig
- Non-Guideline Study, comparable to OECD 471: Positive in Salmonella with and without metabolic activation
- Non-Guideline Study, comparable to OECD 476: Negative in CHO cells with and without metabolic activation
- Non-Guideline Study, comparable to OCED 476: Positive in L5178Y TK+/- cells with and without metabolic activation
- Non-Guideline Study, comparable to OCED 471: Positive in Salmonella with activation
- Non-Guideline Study, comparable to OCED 471: Positive in Salmonella with activation
- Non-Guideline Study, comparable to OCED 471: Positive in Salmonella with activation
- Non-Guideline Study, comparable to EU Method B.21: Negative in BALB/3T3 cell transformation assay with and without activation
- Non-Guideline Study, comparable to OECD 479: Positive in CHO cells with metabolic activation; weakly positive without
- Modified Ames Test according to ASTM E1687-10: Negative in Salmonella with metabolic activation
- Non-Guideline Study, comparable to EPA OTS 798.5915: In Vivo Sister Chromatid Exchange Assay.- Positive in mice via IP injection
- Non-Guideline Study, comparable to EU Method B.3: Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells In Vivo. Positive in rats via oral gavage

[redacted]

- Non-Guideline Study, comparable to EU Method B.12: In Vivo Mammalian Erythrocyte Micronucleus Test. Negative in mice via IP injection
- Non-Guideline Study, comparable to OECD 475: Not clastogenic in rat bone marrow via oral gavage
- Non-Guideline Study, comparable to EU Method B.12: Negative in mice via oral gavage
- EPA OTS 798.4900: Prenatal Developmental Toxicity Study. Sprague-Dawley rats (24 females/dose) had the test substance applied to the skin at concentrations of 0, 0.05, 1, 10, 50, and 250 mg/kg-bw/day for 6hr/d, from GD 0 to GD 19. No maternal deaths, clinical signs, abortions, premature deliveries or irritation observed. Significantly decreased maternal body weight, body weight gain, and food consumption with dose relation. No necropsy findings. Red vaginal discharge and dose-related decrease in gravid uterine weight observed in treated animals at 1 mg/kg/day and higher. Increased number of dead and resorbed fetuses in the 1, 10, and 50 mg/kg/day groups. Decreased fetal bodyweights. Increased incidence of delayed development for soft tissue but no other gross external malformations. Reduction in the extent of ossification of caudal vertebrae, metacarpals, and phalanges at 1, 10, and 50 mg/kg/day. NOAEL for maternal and developmental toxicity = 0.05 mg/kg-bw/day.
- Non-Guideline Study, comparable to OECD 414: Sprague-Dawley rats had the test substance applied to the skin at doses of 0, 4, 8, 30 or 125 mg/kg-bw/day (n=11, 12, 14, 13, or 12 resp.) on GD 0-19. Maternal NOAEL = 4 mg/kg-bw/day based on decreased net body weight gain and the occurrence of vaginal discharge. Developmental NOAEL = 4 mg/kg/day based on decreased live litter size.
- Test Guideline Not Specified: Developmental Toxicity Study. Sprague-Dawley rats (10 females/dose) had the test substance applied to the skin at doses of 0, 4, 8, 30, 125 and 250 mg/Kg/day on GD 0 - 19. Maternal and developmental NOAEL= 8 mg/kg/day based on toxicity at higher doses (vaginal bleeding, a decrease in body weight gain, a reduction in food consumption, and effects on serum chemistry, indicative of liver toxicity; reduced pup size, enlarged brain ventricles, displaced esophagus and anomalous heart development).
- Non-Guideline Study, comparable to OECD 414: Sprague-Dawley rats (12 females/dose) had the test substance applied to the skin at doses of 0, 0.05, 10 or 50 mg/kg-bw/d, for 6 hr/d, on GD 0-20. Maternal NOAEL = 10 mg/kg-bw/day based on decreased body weight/body weight gain, decreased food intake and the occurrence of vaginal bleeding and discharge. Developmental NOAEL = 10 mg/kg/day based on a reduction in total and live litter size, an increased proportion of dead pups and decreased litter weight.
- Non-Guideline Study, comparable to OECD 451: Lifetime Carcinogenicity Study. C3H/HeJ mice (50 males/group) had the test substance in toluene applied to the skin at concentrations of 0, 0.1, 1.0, or 10% twice weekly. Dermal carcinogen in mice
- Test Guideline Not Specified: 25-week Tumor Initiation and Promotion Study. CD-1 mice (30 males/group) had the test substance (in toluene and acetone) applied to the skin at a concentration of 0 or 1% 2x/week for 25 weeks. Tumor initiating activity was observed but the test substance was not a tumor promoter in mice.

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- Non-Guideline Study, comparable to OECD 451: Lifetime Carcinogenicity Study C3H mice (40-50 males/group) had the test substance in white oil applied to the skin at concentrations of 0 or 1-50% three times weekly. Dermal carcinogen in mice; ECHA established a carcinogenicity LOAEL of 5%
- EPA OTS 798.4900: Prenatal Developmental Toxicity Study. Sprague-Dawley rats (24 females/dose) had the test substance in acetone applied to the skin at doses of 0, 1, 10, 50 or 250 mg/kg bw/d, for 6 hr/d on GD 0-19. There were no treatment related deaths or skin irritation. Red vaginal exudate was observed at 50 (60%) and 250 (79%) mg/kg/day. In the 250 mg/kg/day group, 25% of animals appeared emaciated. Decreased body weight gain was observed in treated animals (-28%, -32%, -70% and -88% in 1, 10, 50 and 250 mg/kg/d groups, respectively). Correlating decreased in food consumption were observed (-11%, -14%, -19% or -30%, respectively). Corrected maternal body weight was significantly decreased (-6%, -8%, -16%, -26%, respectively). Corrected maternal body weight gain was significantly decreased (30-70%). There were no gross findings. Gravid uterine weight was significantly decreased in all treated groups and a dose relation was observed (-40%, -64%, -89%, -96%, respectively). NO changes to corpora lutea or implantation sites were observed. A dose-related increase in resorptions (largely early resorptions) was observed at all doses (35-100%). Complete litter loss was significantly increased at 50 and 250 mg/kg/day (83-100% of dams). Live litter sizes were reduced in a dose related manner (14.3, 9.3, 4.9 or 0.9 pups/litter). Fetal body weights were significantly less than controls (14-25%). No increase in fetal malformations was observed. Increased fetal variations were observed. Maternal NOAEL = 1 mg/kg/day based on decreased net body weight/net body weight gain and a reduction in food intake. Developmental NOAEL <1 mg/Kg bw/day based on embryo lethality, decreased fetal body weight, increased resorptions, decreased litter size and retardation of soft tissue and skeletal development.

ChemIDPlus Database:

- Test Guideline Not Specified: LD50(rat)= 4300mg/kg; somnolence, hypermotility, diarrhea
- Test Guideline Not Specified: LD (rabbit) >2000 mg/kg

ChemView Database (NOTE: Some of the studies below may be duplicates of those listed above under ECHA):

- Test Guideline Not Specified: Moderate irritation in rabbits
- Test Guideline Not Specified: 13-week dermal toxicity study in rats. Albino rats had the test substance applied to the skin at doses of 0, 0.001, 0.05, 0.1, and 0.5 ml/kg/day for 13-weeks, 5 days/ week, 6hr/day [assuming a density of ~1, that would be equal to 0, 1, 50, 100 and 500 mg/kg/d] . The test site was occluded after application of the test substance. In the 0.5 ml/kg/day group, nine animals died or were sacrificed in moribund condition. One male in the 0.05 ml/kg/day group was found dead but this was presumed to be due to injuries sustained from wrapping. In the 0.5 ml/kg/day group,

[redacted]

clinical signs such as cold to touch, paleness, lethargy, pale eyes, ears, nose and feet, labored breathing, ataxia, gasping and tremors were observed. Lethargy observed at 0.001 ml/kg/day was considered to be related to dehydration. Yellow anogenital staining in treated groups was determined to be incidental based on the low incidence (n=5, highest incidence days 2-4). Very slight dermal irritation was observed sporadically in treated animals without a dose relationship; therefore, it was not considered related to the test substance. Decreased body weights were observed in 0.5 ml/kg/day females (significant, dose-dependent). Decreased food consumption at this dose was observed, however, this was not considered treatment related due to the lack of clear trends in other groups. Hematology changes (decreased RBC parameters, decreased platelet count, and cellular depletion of the bone marrow were observed in treated groups. No treatment related gross findings were observed. Hyperkeratosis was observed in females at 0.1 and 0.5 ml/kg/day. Acanthosis and epidermal crusting were observed in males at 0.5 ml/kg/day. Decreased terminal body weights were observed in the 0.5 ml/kg/day group. Liver toxicity including hepatic congestion, necrosis, vacuolar change, and alteration in liver blood chemistry was observed at 0.001 ml/kg/day and higher. Thymic atrophy and chronic inflammation of the thymus was observed at 0.001 mg/kg/day and higher. Increased lung weights were also observed at 0.05 ml/kg/day and higher. Dermal irritation NOEL = 0.10 ml/kg/day in males and 0.05 ml/kg/day in females. Systemic NOEL (males) = 0.001 ml/kg/day, NOEL (females) = 0.01 ml/kg/day and LOEL= 0.05 ml/kg/day (~53 mg/kg/day) based on liver toxicity, thymic effects, and increased lung weight.

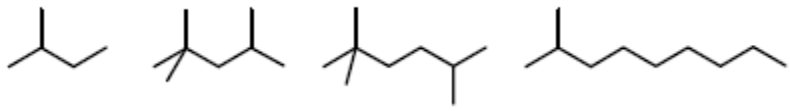
- Test Guideline Not Specified: Developmental toxicity study in rats. Sprague-Dawley rats (10 dams/group) had the test substance applied to the skin at doses of 0, 4, 8, 30, 125, and 250, mg/kg bw/day on GD0-19. In maternal animals, dose related decreases in body weight and food consumption, increases in relative liver weight, vaginal bleeding, atrophy of the thymus (250 mg/kg/day only), abnormal serum chemistry, and decreased litter sizes (mean litter size of 4.8 at 30 mg/kg/day, only 2 fetuses in the 125 mg/kg/day group) were observed as low as 8 mg/kg/day. Increased in utero death of embryo/fetuses were observed (resorptions (%) = 100% at 250 mg/kg/day, 97% at 125 mg/kg/day, and 70% at 30 mg/kg/day). Decreased fetal body weight/crown-rump length was observed at 8mg/kg/day and higher. Dose related external anomalies were observed at 8, 30, and 125 mg/kg/day including: cleft palate, micrognathia, kinked tail, edema. Visceral anomalies observed included enlarged ventricles of the brain, displacement of the esophagus from a left-sided position to a right-sided position, and anomalous development of the heart. Maternal and Developmental NOAEL =4 mg/kg/day.
- Test Guideline Not Specified: Developmental toxicity study in rats. Sprague-Dawley female rats (11-14/group) had the test substance applied to the skin at doses of 0, 0.05, 10, or 250 mg/kg/day beginning one week prior to mating, through mating, and up to GD20. In maternal animals, increased incidence of vaginal discharge was observed at 250 mg/kg/day. Decreased body weight, body weight change and food consumption

[redacted]

were observed at 10 and 250 mg/kg/day. Thymus size was decreased at 250 mg/kg/day. No females in the 250 mg/kg/day group delivered litters. No other treatment related effects were observed. Maternal NOAEL = 0.05 mg/kg/day and Developmental NOAEL = 10 mg/kg/day.

- Test Guideline Not Specified: Developmental toxicity study in rats. Rats (Crl:SD) had the test substance applied to the skin at doses of 0, 1, 50, or 250 mg/kg/day on GD 0-2, 3-5, 6-8, 9-11, 12-14, 15-17, or 18-19. Increased resorptions were observed in dams dosed on GD6-8 in the high-dose group (3.8 vs 1.1 controls) and mid-dose group (2.0 vs 1.1). Increased resorptions were also observed in dams treated on GD9-11 at the high dose (2.7 v 1.1). A decrease in litter size at the high dose group was observed on dosing days 3-5 and 6-8, the former was attributed to increased preimplantation loss. Decreased body weights and food consumption were observed in dams in all treated groups. No treatment related changes on gross fetal examinations were observed. NOAEL = 1 mg/kg/day based on increased number of resorptions.
- Test Guideline Not Specified: Developmental toxicity study in rats. Sprague-Dawley rats had the test substance applied to the skin at doses of 0, 50, or 250 mg/kg/day on GD 5-11. Reduced body weights and body weight gain were observed in dams at 250 mg/kg/day. Changes in maternal organ weights were also observed. Increased resorptions and subsequent reduced live litters were observed. A statistically significant decrease in ovarian corpora lutea was observed at 250 mg/kg/day which was suggested to be evidence of early pre-implantation loss or reflective of the increased resorption rate given there were no changes among groups in preimplantation loss or number of implants/litter. No significant differences in external fetal malformations or variations were observed.

F.2.6 Naphtha (petroleum), light alkylate, CASRN 64741-66-8



Tier 2 Analogous Mixture

EPA Hazard Characterization, Gasoline Blending Streams, 2011
Data for Naphtha (petroleum), light alkylate (CASRN 64741-66-8):
Acute Toxicity:

- Paraffins: 99.4% (v/v), Olefins: 0%, Naphthenes: 0.6%, Aromatics: 0%

  Test Guideline Not Specified: Acute oral toxicity: Sprague-Dawley rats (5/sex/dose) were administered naphtha (petroleum), light alkylate (API 83-19) via an unspecified oral route at 5000 and 7000 mg/kg-bw and observed for 14 days following dosing. Mortality was observed in one female at 5000 mg/kg-bw. LD50 > 7000 mg/kg
- Paraffins: 99.4% (v/v), Olefins: 0%, Naphthenes: 0.6%, Aromatics: 0%

[redacted]

Test Guideline Not Specified: Acute inhalation toxicity: Sprague-Dawley rats (5/sex/dose) were exposed whole-body to naphtha (petroleum), light alkylate (API 83-19) as a vapor at a nominal concentration of 5.04 mg/L for 4 hours and observed for 14 days following exposure. The mean measured concentration was 6.31 mg/L. No mortalities occurred. LC50 > 6.31 mg/L

- Paraffins: 99.4% (v/v), Olefins: 0%, Naphthenes: 0.6%, Aromatics: 0%

  Test Guideline Not Specified: Acute dermal toxicity: New Zealand White rabbits (4/sex/dose) were administered naphtha (petroleum), light alkylate (API 83-19) via the dermal route at 2000 mg/kg-bw on either abraded or intact skin under occluded conditions for 24 hours and observed for 14 days following dosing. No mortalities occurred. LD50 > 2000 mg/kg

Repeated-Dose Toxicity:

- **NOAEC= 24,300 mg/m^3,** no effects observed at the highest concentration tested. Paraffins: 99.97% (v/v), Olefins: 0.03%, Naphthenes: 0%, Aromatics: 0%

  Test Guideline Not Specified: Repeated-dose toxicity: Sprague-Dawley rats (12/sex/dose) were exposed whole-body to naphtha (petroleum), light alkylate distillate (LAN-D) as a vapor at mean measured concentrations of 0, 2.5, 8.2 and 24.3 mg/L, 6 hours/day, 5 days/week for 13 weeks and observed for 4 weeks after the exposure ended. Endpoints included clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, histopathology, neurobehavior and ophthalmoscopy. No mortality was observed. Absolute and relative kidney weights were increased in the males at all dose levels; this correlated with the occurrence of hyaline droplets in the proximal convoluted tubules.[17] Increased absolute and relative liver weights were observed in the high-dose males and females; there were no pathological findings associated with this increase and differences disappeared after the recovery period. No other treatment-related effects were observed. NOAEC = 24.3 mg/L/day (based on no effects observed at the highest concentration tested)

Reproductive Toxicity:

- NOAEC = 25,000 mg/m^3, no effects observed at the highest concentration tested). Paraffins: 99.97% (v/v), Olefins: 0.03%, Naphthenes: 0%, Aromatics: 0% Test Guideline Not Specified: Repeated-dose/Reproductive/Developmental toxicity: In a combined reproductive/developmental toxicity screening test, Sprague-Dawley rats (10/sex/dose) were exposed whole-body to naphtha (petroleum), light alkylate (LAN-D) at nominal concentrations of 0, 5, 12.5 or 25 mg/L as a vapor, 6 hours/day for 7 – 8 weeks,

[17] This is footnote 6 from the EPA 2011 Hazard Characterization: "Nephropathy seen in male rats may be occurring by an alpha 2μ-globulin-mediated mechanism (which is male rat-specific and not considered relevant to humans). EPA's Risk Assessment Forum has outlined key events and data that are necessary to demonstrate this mode of action (Alpha 2μ-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Rat, EPA/625/3-91/019F)."]

[redacted]

including 2 weeks prior to mating, during mating and gestation, and up to postpartum day 4. Exposure of females was suspended on gestation day 19. Measured concentrations were between 96 and 104% of nominal concentrations. No treatment-related mortalities were observed. There were no effects on parental body weights, food consumption, organ weights, number of pregnant females, number of animals delivering, number of corpora lutea, number of implantation sites, number of pups born, live born index, viability index, sex ratio, clinical observations of pups and pup body weights. NOAEC (reproductive toxicity) = 25 mg/L/day (based on no effects observed at the highest concentration tested)

Developmental Toxicity:

- Paraffins: 99.97% (v/v), Olefins: 0.03%, Naphthenes: 0%, Aromatics: 0%

  Test Guideline Not Specified: In the combined reproductive/developmental inhalation toxicity screening test in Sprague-Dawley rats described previously, no effects were observed on the number of corpora lutea, number of implantation sites, number of pups born, live born index, viability index, sex ratio, clinical observations of pups, pup body weights and body weight gain. No treatment-related effects were observed on the incidence of visceral and skeletal abnormalities in pups on day 4 postpartum. NOAEC (maternal and developmental toxicity) = 25 mg/L/day (based on no effects observed at the highest concentration tested)

Genotoxicity:

- Paraffins: 99.4% (v/v), Olefins: 0%, Naphthenes: 0.6%, Aromatics: 0%

  Test Guideline Not Specified: Genotoxicity: Mouse lymphoma L5178Y TK+/- cells were exposed to naphtha (petroleum), light alkylate (API 83-19) in acetone at concentrations of 0.005 – 0.08 µg/mL without metabolic activation or 0.00004 – 0.8 µg/mL with metabolic activation. Positive and negative controls responded appropriately. Complete toxicity was observed at 0.05 µg/mL without activation and 0.5 µg/mL with activation. Naphtha (petroleum), light alkylate (API 83-19) did not cause an increase in mutation frequency. Naphtha (petroleum), light alkylate was not mutagenic in this assay.

- Paraffins: 99.4% (v/v), Olefins: 0%, Naphthenes: 0.6%, Aromatics: 0%

  Test Guideline Not Specified: Genotoxicity: In a bone marrow chromosomal aberration assay, Sprague-Dawley rats (15/sex/dose) were administered naphtha (petroleum), light alkylate (API 83-19) in corn oil at concentrations of 0, 0.3, 1.0 or 3.0 g/kg-bw via intraperitoneal injection and sacrificed up to 48 hours later. Positive and negative controls responded appropriately. There were no treatment-related increases in chromosomal aberrations.

[redacted]

Skin Irritation:

- Paraffins: 99.4% (v/v), Olefins: 0%, Naphthenes: 0.6%, Aromatics: 0%

  Test Guideline Not Specified: Skin irritation: Six rabbits (strain and sex not specified) were administered 0.5 mL of naphtha (petroleum), light alkylate (API 83-19) to intact or abraded skin under occluded conditions for 24 hours and observed for 14 days following dosing. Erythema and edema were observed on both intact and abraded skin. The primary dermal irritation index was 3.9. Naphtha (petroleum), light alkylate was **moderately irritating** to rabbit skin in this study.

Eye Irritation:

- Paraffins: 99.4% (v/v), Olefins: 0%, Naphthenes: 0.6%, Aromatics: 0%

  Test Guideline Not Specified: Eye irritation: Rabbits (9/dose; strain and sex not specified) were administered 0.1 mL of naphtha (petroleum), light alkylate (API 83-19) to one eye; the other eye served as a control. After 20 – 30 seconds, the treated eyes of three rabbits were rinsed with water for 1 minute. Animals were observed for 7 days after treatment. No corneal or iridial irritation was observed. Naphtha (petroleum), light alkylate was not irritating to rabbit eyes in this study.

Skin Sensitization:

- Paraffins: 99.4% (v/v), Olefins: 0%, Naphthenes: 0.6%, Aromatics: 0%

  Test Guideline Not Specified: Skin sensitization: Guinea pigs (10/sex, strain not specified) were administered 0.4 mL of 50% naphtha (petroleum), light alkylate (API 83-19) in paraffin oil to shorn skin under occluded conditions for 6 hours once per week for 3 weeks. After a 2-week resting period, a challenge dose of 0.4 mL of 25% test substance in paraffin oil was applied to a previously untreated site, and animals were observed for 48 hours following treatment. A very slight erythema was observed in one animal after the challenge dose; the remaining treatment animals exhibited no response. A similar response was observed in control animals. Naphtha (petroleum), light alkylate was not sensitizing to guinea pig skin in this study.

Carcinogenicity:

- Paraffins: 99.4% (v/v), Olefins: 0%, Naphthenes: 0.6%, Aromatics: 0.1%

  Test Guideline Not Specified: Carcinogenicity: C3H/HeJ mice (50 males) were administered 0.05 mL of naphtha (petroleum), light alkylate (API 83-19) via the dermal route 2 times/week to clipped skin for 104 weeks. No effects were observed on the incidence of tumors. Naphtha (petroleum), light alkylate was not carcinogenic to mice in this study.

Neurotoxicity:

- Paraffins: 99.97% (v/v), Olefins: 0.03%, Naphthenes: 0%, Aromatics: 0%

  Test Guideline Not Specified: Neurotoxicity. In the repeated-dose inhalation study described previously, Sprague-Dawley rats exposed to naphtha (petroleum), light

[redacted]

alkylate distillate (LAN-D) as a vapor were subjected to neurobehavioral measurements, including motor activity and functional observational battery tests. No treatment-related effects were observed on neurobehavior. Naphtha (petroleum), light alkylate was not neurotoxic to rats in this study.

ECHA Database:

Repeated-Dose Toxicity:

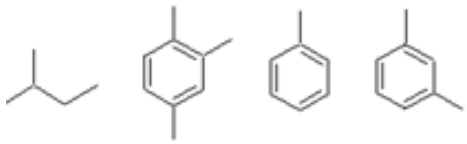
- **LOAEL for systemic toxicity: 500 mg/kg/day.** Test Guideline Not Specified: 28-day oral toxicity study in male Fischer 344 rats via gavage. Four naphtha streams (light catalytic cracked naphtha, CASRN 64741-55-5; light catalytic reformed naphtha, CASRN 64741-63-5; heavy catalytic cracked naphtha, CASRN 64741-54-4; and light alkylate naphtha, CASRN 64741-66-8) and fifteen pure hydrocarbons were tested at doses of 500 or 2000 mg/kg/day for 5 days/week for 4 weeks. The concurrent negative control group was administered saline at 2000 mg/kg/day and a concurrent positive control group was administered an unleaded gasoline sample at 500 or 2000 mg/kg/day. Naphtha treatments were administered neat (no vehicle). Rats were observed twice daily for mortality and clinical signs and all animals found dead or moribund were subjected to gross necropsy. Body weights were assessed only prior to dosing on Day 1 and at scheduled sacrifice. At the conclusion of the exposure period, kidneys were weighed and fixed and histopathological examinations were limited to grading severity of three specific kidney histopathological observations: (1) foci of regenerative epithelium in the renal cortex; (2) foci of intratubular cast formation located between the inner and outer stripe of the renal medulla; and (3) hyaline droplet accumulation within the epithelial cells of the proximal convoluted tubules. The severity scores of these three kidney observations were manipulated to produce a "nephropathy score" for each individual animal. All tissues other than the kidney were discarded after gross necropsy and not assessed for histopathology. It was reported that lethargy was the primary clinical sign of toxicity in this study. Portal-of-entry effects of the stomach (including erythema, erosion of the gastric mucosa, raised discolored foci on the gastric epithelial lining, and ulceration) were observed upon gross necropsy and appeared to be generally dose-related. Kidney and liver lesions observed upon gross necropsy included discoloration and mottling, which were postulated by the study authors to be due to post-mortem changes, as the changes were mainly observed in animals with unscheduled deaths. The observations of lethargy and stomach, kidney, and liver gross necropsy findings were reported as summarized findings for the entire study; it was not reported which test substances and at which doses these findings were observed. It is not possible to determine which test substances at which doses resulted in lethargy and the stomach, kidney, and liver gross necropsy findings based on the data provided. For animals treated with light alkylate naphtha, mortality was 10% at 500 mg/kg/day and 20% at 2000 mg/kg/day, body weights were significantly decreased relative to control at 2000

[redacted]

mg/kg/day, nephropathy scores were significantly increased ≥ 500 mg/kg/day, and kidney weights were unaffected. It was stated that animals deaths in low-dose test groups prior to Day 14 (unclear if this applies to the light alkylate naphtha-treated animals) were either due to toxicity of the test substance or from gavage error; based on this description, it is unclear whether the death in the light alkylate naphtha-treated group at 500 mg/kg/day was treatment-related. The kidney histopathological findings were stated by the study authors to be indicative of alpha-2u-nephropathy and therefore specific to male rats and not relevant to humans. For light alkylate naphtha (CASRN 64741-66-8), a LOAEL of 500 mg/kg/day was established based on mortality; a NOAEL was not established. (ECHA)

- **NOEL for systemic toxicity: 2000 mg/kg/day. NOEL for dermal irritation <200 mg/kg/day.** Non-guideline study but comparable to OECD 410: Repeated Dose Dermal Toxicity: 28-Day Study in Rabbits at doses of 0, 200, 1000, or 2000 mg/kg for 4 weeks. The test substance was dermally applied to New Zealand White rabbits (5/sex/dose) at doses of 0, 200, 1000, or 2000 mg/kg for 6 hours for 3 times/week for 4 weeks. Cage side observations and detailed clinical observations occurred twice daily. Signs of dermal irritation were recorded, and body weights were measured. Blood was collected prior to the study at termination for hematology and clinical chemistry. Gross and histopathological examinations were conducted. There were no mortalities. Four high dose females appeared thin and the effect was considered treatment related. Moderate to severe dermal irritation was observed in the mid and high dose groups and was dose-dependent. Significantly lower mean body weight gains were observed compared to controls (dose group not specified). Dry, scaly, rough, fissured, reddened, crusted and/or thickened skin were observed at the treated sites. Proliferative and inflammatory changes of the skin were observed in all high dose animals. Increased granulopoiesis of the bone marrow was also observed in the high dose group. A NOEL of < 200 mg/kg/day was established for dermal irritation. A NOEL of 2000 mg/kg/day was established for systemic toxicity based on no adverse effects. (ECHA)

F.2.7 Naphtha, petroleum, heavy catalytic reformed, CASRN 64741-68-0



Tier 2 Analogous Mixture

8(e) Database:

- Acute inhalation toxicity: LC50 (rats) = 31.1 mg/L (males), 23.9 mg/L (females); coma, ataxia.

[redacted]

- Repeated dose inhalation toxicity: 15/20 rats died at a dose of 10 mg/L (administered 6 hrs/day for 3 weeks); salivation, lacrimation, coma, ataxia, decreased motor activity, decreased breathing rate, focal/multifocal congestion, edema, and interstitial pneumonia for the lungs, corneal ulceration and/or necrosis.

ECHA Database

- Test Guideline Not Specified: 21-day repeated dose inhalation toxicity study in rats. Sprague-Dawley rats (10/sex/dose) were exposed to the test substance as vapor at concentrations of 0 (chamber air), 0 (animal room), 1.03, 2.81, or 10.20 mg/L (~0, 1030, 2810, or 10,200 mg/m3; ~0, 215, 587, 2132 ppm) for 6 hours/day, 5 days/week, for 21 days. Animals were sacrificed following the exposure period, and general toxicity and kidney effects were evaluated, with the results focusing on kidney effects. Mortalities occurred in the highest dose group (number not specified) and were attributed to pulmonary toxicity (interstitial pneumonitis and pulmonary edema). There were no adverse renal effects. No additional results reported. A NOAEC of 2810 mg/m^3 and a LOAEC of 10200 mg/m^3 were established based on pulmonary toxicity deaths at the highest dose. A NOAEC of 10200 mg/m3 was established for renal toxicity based on a lack of adverse effects at the highest dose tested. (HPVIS)

EPA Hazard Characterization, Gasoline Blending Streams, 2011
Data for Naphtha (petroleum), heavy catalytic reformed (CASRN 64741-68-0)
Repeated-Dose Toxicity:

- Paraffins: 33.6% (v/v), Olefins: 1.3%, Naphthenes: 3.3%, Aromatics: 58.1%
  Test Guideline Not Specified: Repeated-dose toxicity: Sprague-Dawley rats (10/sex/dose) were administered naphtha (petroleum), heavy catalytic reformed (F-184) via the dermal route at 0, 0.05, 0.25 or 1.0 mL/kg-bw (~ 0, 40, 199 or 797 mg/kg-bw) under occluded conditions, 6 hours/day, 5 days/week for 28 days. Endpoints included clinical signs, body weights, organ weights, hematology, clinical chemistry and histopathology. No study-related mortalities occurred. Slight to moderate dermal irritation, as evidenced by grossly visible lesions and by microscopic histopathological changes in the skin, was observed at a dose of 797 mg/kg-bw/day. Slight dermal irritation was noted at a dose of 199 mg/kg-bw/day and very slight dermal irritation was noted at a dose of 40 mg/kg-bw/day. No treatment-related effects were observed in any other parameters. NOAEL ~ 797 mg/kg-bw/day (based on no systemic effects at the highest dose tested).

Genotoxicity:

- Paraffins: 9.4% (v/v), Olefins: <0.1%, Naphthenes: 0.1%, Aromatics: 89.8%
  Test Guideline Not Specified: Genotoxicity: Mouse lymphoma L5178Y TK+/- cells were exposed to naphtha (petroleum), heavy catalytic reformed (API 83-06) in ethanol at concentrations of 18 – 75 nL/mL without metabolic activation and 67 and 220 nL/mL with activation. Both positive and negative controls responded appropriately. An increase in mutation frequency was observed at high concentrations both with and

without activation. The response was judged to be equivocal because the growth of cultures was below 10% without activation and the positive response was not reproducible with activation. Naphtha (petroleum), heavy catalytic reformed was equivocal for the induction of mutations in this assay.

- Paraffins: 9.4% (v/v), Olefins: <0.1%, Naphthenes: 0.1%, Aromatics: 89.8%
  Test Guideline Not Specified: Genotoxicity: Mouse lymphoma L5178Y TK+/- cells were exposed to naphtha (petroleum), heavy catalytic reformed (API 83-06) at unspecified concentrations with and without activation. Naphtha (petroleum), heavy catalytic reformed (API 83-06) was mutagenic with activation only. No other details were provided. Naphtha (petroleum), heavy catalytic reformed was mutagenic in this assay.

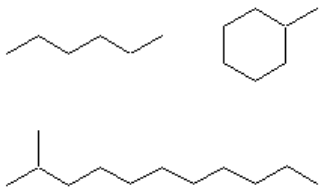
Skin Irritation:

- Paraffins: 33.6% (v/v), Olefins: 1.3%, Naphthenes: 3.3%, Aromatics: 58.1%
  Test Guideline Not Specified: Repeated-dose toxicity: In the dermal repeated-dose study in Sprague-Dawley rats described previously, administration of naphtha (petroleum), heavy catalytic reformed (F-184) at a dose of 1.0 mL/kg-bw/day resulted in slight to moderate dermal irritation, as evidenced by grossly visible lesions and by microscopic histopathological changes in the skin. Slight dermal irritation was noted at a dose of 0.25 mL/kg-bw/day and very slight dermal irritation was noted at a dose of 0.05 mL/kg-bw/day. Naphtha (petroleum), heavy catalytic reformed was moderately irritating to rat skin in this study.

Carcinogenicity:

- Paraffins: 9.4% (v/v), Olefins: < 0.1%, Naphthenes: 0.1%, Aromatics: 89.8%
  Test Guideline Not Specified: Carcinogenicity: C3H/HeJ mice (50 males) were administered 0.05 mL of naphtha (petroleum), heavy catalytic reformed (API 83-06) via the dermal route 2 times/week to clipped skin for 104 weeks. No effects were observed on the incidence of tumors. Naphtha (petroleum), heavy catalytic reformed was not carcinogenic to mice in this study.

F.2.8 Naphtha (petroleum), heavy hydrocracked, CASRN 64741-78-2



Tier 2 Analogous Mixture

ECHA Database

- NGS; comparable to OECD 410: Repeated Dose Dermal Toxicity: 28-Day Study in Rats.
  The test substance was administered to male and female Sprague-Dawley rats (10/sex/dose) at doses of 0, 7.5, 37.5, or 375 mg/kg-bw, 6 hours/day, 5 days/week, for 4

[redacted]

weeks. Control animals were sham-exposed. Very slight to moderate dermal irritation was noted during the study at the first dose site. Slight dermal irritation was observed at the second dose site. No animals died or were sacrificed moribund during the observation period. No test article-related differences noted between dose and sham group body weights. No significant differences were noted between the sham control and treated group values in any of the hematology parameters tested. No significant differences were noted between the sham control and treated group values in any of the clinical chemistry parameters tested. No significant differences in organ weights noted between the does and sham groups. Treatment-related findings noted in the skin of animals from the mid- and high-dose groups at the time of necropsy included dried skin and eschar. There was an increased incidence of these findings in the high dose group when compared to mid-dose group. Non-dermal findings included enlarged cervical lymph nodes in a male of the sham control group, an adhesion on the cerebrum of a female from the sham control group and a cyst on an ovary of a female from the 0.05 ml/kg does group. Since the non-dermal findings occurred in low incidence and only in the sham control and low dose groups, they are not considered to be treatment-related. Histopathology findings indicate that the application of this article induced mild epidermal irritation at the high dose site. The NOEL for dermal irritation was 7.5 mg/kg-bw/day. The NOEL for systemic effects was > 375 mg/kg-bw/day [ECHA]

F.2.9 Extracts (petroleum), light paraffinic distillate solvent, CASRN 64742-05-8

Structure not available

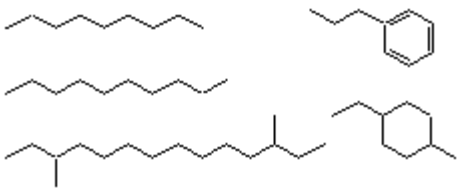
Tier 2 Analogous Mixture

Health Canada Screening Assessment Petroleum Sector Stream Approach for Distillate Aromatic Extracts (2017):

- OECD 411: 90-day dermal study in rats. The test substance was dermally applied to Sprague-Dawley rats (20/sex/dose) at doses of 0, 5, 50, or 150 mg/kg/day for6 hours/day, 5 days/week for 90 days. There were no treatment-related effects on clinical toxicity, dermal effects, food consumption, or ophthalmic, macroscopic, or microscopic findings. Decreased body weight gains were observed in the high dose females, which resulted in slightly lower body weight (8.1%) compared to controls at week 12. Decreased red blood cell counts, hemoglobin, hematocrit, activated partial thromboplastin time, white blood cell counts, lymphocytes, eosinophils, platelet counts and increased red cell distribution widths and hemoglobin distribution widths were observed in the mid and high dose groups. Increased absolute reticulocyte counts were observed in high dose males and increased mean reticulocyte percentage was observed in high dose females. Decreased eosinophil counts were observed in low dose females. Increased cholesterol, sorbitol dehydrogenase, blood urea nitrogen, alanine aminotransferase and triglycerides levels were observed in the mid and high dose groups. There were effects on spleen, liver, thymus, pituitary, heart, and thyroid/parathyroid weights in the mid and high dose groups (effect not specified if change was an increase or decrease). LOAEL = 5 mg/kg-bw/day based on lower eosinophil counts in females.

[redacted]

F.2.10 Distillates, petroleum, hydrotreated light, CASRN 64742-47-8



Tier 2 Analogous Mixture

OECD SIAP:

- OECD 401: LD50 (rats) > 5000-15800 mg/kg
- OECD 402: LD50 (rats or rabbits) > 2000 mg/kg
- TGNS: Not irritating – minimally irritating in rabbits
- TGNS: Not irritating – minimally irritating in rabbits
- TGNS: Not sensitizing in humans
- OECD 471: Negative with and without metabolic activation
- OECD 473: Negative with and without metabolic activation

ECHA Database:

- Comparable to OECD 413: 13 week repeated dose inhalation toxicity study in rats. Whole body concentrations of 0.02, 0.048, and 0.10 mg/L for 6 hrs/day, 5 days/wk, for 13 weeks. NOAEL ≥ 0.1 mg/L in males based on a lack of adverse treatment related effects at the highest dose tested.

8e Database:

- [redacted]
- The test material was administered ora1ly, by gavage, to groups of 10 male and 10 female rats 7 days per week for 13 weeks followed by a 4 week recovery period. The doses used were 0 (control), 500, 2500 or 5000 mg/kg/d. There were daily observations for mortality and signs of toxicity; weekly body weight and feed consumption measurements and complete necropsy observations at the conclusion of the study. Additional measurements included hematology and serum chemistry at the conclusion of the dosing interval and at the end of the recovery period. At necropsy the principal organs were removed and weighed. Histopathological observations were made of 40 tissues and organs from all animals in the control and high-dose group with target organs evaluated in the other test groups.

Clinical Observations:

The majority of the animals in the control, low- and mid-dose groups displayed no observable abnormalities during the test period. In the high-dose group, there was a dramatic increase in the incidence of swollen anus, anogenital staining, emaciation, and

[redacted]

alopecia. During the recovery period, the incidence of abnormal signs decreased over time with an increase in the number of animals exhibiting no observable abnormalities.

Mean Body Weight:

Mean body weights of the high-dose male rats were significantly less than control ($p \leq 0.05$) at Day 42 and until study termination ($p \leq 0.01$). The mean body weights of the mid-dose male rats were also less ($p \leq 0.05$) on Day 77 until study termination. The mean body weights of the female rats were significantly less than control ($p \leq 0.05$) at the mid-dose on Day 91 and at the high-dose on Days 77 and 91. Both the mid and high-dose female rats were significantly lighter ($p \leq 0.01$) at study termination. Associated with these body weight changes were significant decreases in feed consumption at the mid- and high-dose for both male and female rats.

Hematologic Parameters:

Platelet count was significantly elevated in the low-dose males ($p \leq 0.05$) and the mid- and high-dose males ($p \leq 0.01$). Other hematologic parameters in males which differed from controls were found only in the mid-dose: hematocrit ($p \leq 0.01$), hemoglobin ($p \leq 0.01$), mean corpuscular volume ($p \leq 0.05$), and mean corpuscular hemoglobin ($p \leq 0.05$). In females, the only hematologic parameter which significantly differed from controls was the platelet count in the high-dose ($p \leq 0.01$). After the recovery period, there were no significant differences in the hematologic parameters in any of the dose groups as compared to the control group.

Serum Chemistry:

In male rats, serum glucose was significantly decreased at all doses. At the mid- and high-doses, urea nitrogen, alanine aminotransferase and cholesterol were significantly increased, and at the high dose total bilirubin and gamma-glutamyl transferase were significantly elevated. In female rats at the mid- and high-dose, serum glucose and chloride were significantly decreased and cholesterol was increased. After the recovery period, there were no differences between male and female test groups and the corresponding controls.

Organ Weights: The following statistically significant organ weight changes were noted. In males, absolute and relative kidney weights and absolute liver weights were increased at all dose levels. In females, relative kidney weights and absolute liver weights were increased at all dose levels. Relative liver weights were increased in males and females at both the mid- and high-doses. Absolute and relative adrenal weights were increased in males at the high-dose and in females at the mid- and high-dose levels. Additionally, testes weights were increased at the high-dose.

Histopathology:

Treatment-related microscopic changes were observed in the kidneys of male rats at all dose levels of the aliphatic hydrocarbon, the liver of male and females at all dose levels, and the stomach and/or anus of males and females at 2500 and 5000 mg/ kg . Histopathologic examination of the kidneys of male rats showed changes typical of

[redacted]

hyaline droplet nephropathy, with essentially no difference in the incidence and/or severity of the lesions among the exposed groups. These renal changes consisted of accumulation of hyaline droplets in the cytoplasm of the proximal convoluted tubules, dilatation and granular cast formations in the medullary tubules and increased basophilia of cortical tubules. These affected basophilic cortical tubules showed changes consistent with both degeneration and regeneration. By the end of the recovery period, there was no evidence of hyaline droplets in the cortical tubules, but there were dilated tubules with granular casts in the medulla of 4/ 8 male rats. There was no difference in the incidence of cortical basophilic tubules between the control and the treated groups. No significant histopathologic changes were observed in any of the female rats. The treatment -related effect in the liver of both male and female rats consisted of hepatocellular hypertrophy, predominantly in the centrilobular areas. The incidence and intensity of this centrilobular hepatocellular hypertrophy generally occurred in a dose-related manner. This hepatocellular hypertrophy completely disappeared after the recovery period. Histopathologic examination of the stomach showed a thickening of the non-glandular mucosa due to hyperplasia and hyperkeratosis of the squamous epithelium, the incidence and severity of which occurred in a dose -dependent manner. Other associated gastric changes seen at a low incidence in a few of the affected rats included edema and inflammatory cell infiltrations in the submucosa and focal necrosis of the superficial glandular mucosa. After the recovery period, the three female rats showed no residual changes, but 3/8 male rats still had a minimal to slight hyperplasia and hyperkeratosis of the mucosa of the non-glandular area of the stomach (the incidence and severity was decreased).

At necropsy, the anus of most of the male and female rats of the high-dose was described as being swollen. Microscopically, the skin and mucosa around the anus of these rats was thickened due to hyperplasia and hyperkeratosis. Also, there were areas of necrosis, neutrophilic inflammatory cell infiltrations and pustular formations in the superficial mucosa and epidermis of the anus and skin around the anus. These changes were not seen after the recovery period.

Study Author's Conclusions:

The findings of importance are failure to gain weight and an associated decrease in feed consumption: reduction in certain blood values, changes in serum chemistry and increased organ weights. The histopathology was largely confirmatory of the other observations. Mechanistically, we believe there are two simultaneous events occurring. There is the well-known male rat nephropathy associated with aliphatic hydrocarbons. From the organ weight and pathology data, the effect is less severe than with other hydrocarbons. The second effect appears to be the direct result of high-dose intubation of a locally irritating substance. We believe the aliphatic hydrocarbon at the doses employed produced irritation of the gastrointestinal tract. They led to decreased food consumption and resultant reduction in blood components, serum chemistry and enzyme changes and the reversible liver enlargement. The platelet changes and adrenal enlargement could also be a part of this picture. This type of study has not been done

[redacted]

before and the high gavage doses (up to 5000 mg/ kg body weight/ day) are outside our prior experience.

F.2.11 Naphtha (petroleum), hydrotreated heavy C9-C11 alkanes/cycloalkanes, CASRN 64742-48-9

Structure Not Available

Tier 2 Analogous Mixture – Data presented below are taken from the listed databases and represent experiments on similar mixtures that were considered appropriate for CASRN 64742-48-9 by the OECD category document for C9-14 aliphatics with less than 2% aromatics and the ECHA dossier for CASRN 64742-48-9

OECD SIDS/ECHA**:**

- According to or similar to OECD 401: LD50 (rats) > 5.0 g/kg
- According to or similar to OECD 402: LD50 (rabbits or rats) > 2.0 g/kg
- Test Guideline Not Specified: Minimal to slight irritation in rabbits
- Test Guideline Not Specified: Minimal to slight irritation in rabbits
- OECD 471: Negative in S. typhimurium with and without activation
- OECD 408: 90-day repeated oral toxicity test in Sprague-Dawley rats. The study included a 28-day recovery period for rats exposed to the highest dose of 5000 mg/kg/day. NOAEL = 5000 mg/kg/day (highest concentration tested). No additional information provided.
- OECD 413: 90-day inhalation toxicity study in Sprague-Dawley rats. Doses not reported. NOAEC= 5220 mg/m3 (900 ppm), (highest concentration tested). No additional information provided.
- OECD 412: 28-day inhalation toxicity study in Rhesus monkeys. Doses not reported. NOAEC = 4200 mg/m3 (615 ppm), (highest concentration tested). No additional information provided.
- Test Guideline Not Specified: 3-day inhalation test in rats. “Rats were exposed to Hydrocarbons, C9-C11, cyclics, <2% aromatics (CASRN 64742-48-9) test atmosphere for 8 hours/day for 3 consecutive days at 0 (air), 1000 mg/m3 (170ppm), 2500 mg/m3 (430ppm), 5000 mg/m3 (860ppm). All rats were checked for health and viability at least once daily. Body weight was recorded during randomization on days of testing. Results of the behavioral tests indicated only minimal effects of exposure to a C10 cycloparaffinic solvent on neurobehavioral measures at the highest dose tested (5000 mg/m3) including gait abnormalities and psychomotor slowing. Short-term high level exposure to Hydrocarbons, C 9-C11, cyclics, <2% aromatics induced mild and non-persistent neurobehavioral effects on functional observations and measures of learned performance. Minimal effects were observed during or after 3 consecutive 8 hour exposures to Hydrocarbons, C 9-C11, cyclics, <2% aromatics at an exposure level of 5000 mg/m3. Exposure to 1000 or 2500 mg/m3 on a group basis did not induce exposure-related neurobehavioral effects. The effects are consistent with narcosis and the NOAEC = 2500 mg/m3.”

[redacted]

- Non-Guideline Study; comparable to OECD 414: "The test material was administered to pregnant female Sprague-Dawley rats by inhalation exposure to vapor concentrations of 0, 300 or 900 ppm (5220 mg/m3), 6 hours/day during gestation days 6 to 15 to assess developmental toxicity. Included in this study was a negative control (chamber exposed) group and a positive control group that was treated via gastric intubation on gestational days 6 -15 with 400mg/kg/day of acetylsalicylic acid. All surviving females were sacrificed on Day 21 of gestation and fetuses were examined for external, soft tissue and skeletal malformations. Maternal Effects. Animals treated with 900 ppm exhibited a slight increase in excessive lacrimation during the treatment and post-treatment periods. This same group also exhibited an increased incidence of brown flakes in the fur covering the head area during the treatment period. Premature delivery of the litter on Day 21 of gestation prior to maternal sacrifice was observed in one negative control female, and two test material treated females. There were no remarkable gross postmortem changes in the treated adult females. All other physical observations occurred with similar frequencies in all groups and were considered to represent common observations noted in rats in the laboratory environment. Positive control animals demonstrated maternal toxicity. Embryotoxic / Teratogenic effects. All fetal survival, size and sex data for groups treated with test material were comparable to negative control data. Slight delays or variation in the normal ossification process were observed in treated animals. However, such variations are common as the time of normal ossification can vary and were comparable to the variation observed in the control animals. The incidence of fetuses with external malformations and incidences of litters containing malformed fetuses in the groups treated with test material were considered comparable to the control data. No significant difference in the incidence of visceral malformations was observed in the treated groups. The incidence of fetuses with soft tissue malformation in groups treated with test material was comparable to the negative control. Positive control animals demonstrated developmental toxicity. Pregnancy rate, mortality, body weight gain and gross postmortem observations were unaffected by treatment. Hydrocarbons, C9-C11, normal paraffins, isoalkanes, cyclics, < 2% aromatics treatment at either dose level had no effect on reproductive endpoints, fetal size, sex distribution, ossification variation, or fetal examination endpoints. Thus, there was no evidence of maternal or fetal toxicity at either exposure level of Hydrocarbons, C9-C11, normal, isoalkanes, cyclics, < 2% aromatics tested. Based on these results, both the maternal and developmental NOAELs were greater than or equal to 900 ppm (5220 mg/m3)."

HPVIS Database:

- Non-Guideline Study: LD50 (rat) > 6000 mg/kg; perianal soiling, dry material around mouth, soft feces
- Non-Guideline Study: LC50 (rat) > 8500 mg/m3; nasal and ocular discharges, CNS effects, (hyperexcitablility, twitching, circling)

[redacted]

ChemView Database:

- Test Guideline Not Specified: LC50 (rats) = 184 - 319 ppm (1.1 - 1.9 mg/L); mortalities in first 3 days post-exposure
- Test Guideline Not Specified: LC50 (rat) = 279 ppm; ataxia, increased respiration, labored breathing and lethargy
- Test Guideline Not Specified: LC50 (rat) <500 ppm; all animals died at lowest concentration decreased activity, rapid respiration, labored breathing

F.2.12 Fuels, diesel, CASRN 68334-30-5

Structure Not Available
Tier 2 Analogous Mixture
ECHA Database:

- Non-Guideline Study, comparable to OECD 420: oral LD50 (rats) = 21 mL/kg oily urine stains and diarrhea, hair loss, irritation, redness, sores
- TGNS: LC50 (4-hr, rats) > 6000 mg/m3
- Non-Guideline Study, comparable to OECD 404: Irritating in rabbits
- Non-Guideline Study, comparable to OECD 405: Not irritating in rabbits
- Non-Guideline Study, comparable to OECD 406: Not sensitizing in guinea pigs
- Non-Guideline Study, comparable to OECD 476: Negative in mouse lymphoma L5178Y cells with and without metabolic activation
- TGNS: Modified Ames Test. Negative in Salmonella with activation (
- Non-Guideline Study, comparable to OECD 471: Negative in Salmonella with and without metabolic activation
- Non-Guideline Study, comparable to OECD 475: Positive in rats via IP route
- Non-Guideline Study, comparable to OECD 471: Negative in Salmonella with and without metabolic activation
- Non-Guideline Study, comparable to OECD 413: 90 -day inhalation toxicity study in rats. Sprague-Dawley rats (number per group not specified) were exposed to the test substance as an aerosol at nominal concentrations of 0.25, 0.75, or 1.50 mg/L (analytical of 0.35, 0.88, 1.71 mg/L) via whole body inhalation twice a week for 13 weeks. Sham control (n=24) and untreated controls (n=12) were included. Systemic NOAEC > 1.71 mg/L based on no adverse effects at the highest dose tested. Local NOAEC = 0.88 mg/L based on increased relative lung weights.
- Test Guideline Not Specified: Repeated dose study in rats. Sprague-Dawley rats (4/sex/group, 8 in sham control) were exposed to the test substance as an aerosol (percent of fuel in the vapor phase was 15-20%) via whole body inhalation for 2 or 6 hours, once, twice, or three times per week for a total of 9 exposures. No POD established. Body weight loss, mortality, and lung effects (increased pulmonary free cell number, lung weight, and decreased lung volume)
- Test Guideline Not Specified: Repeated dose study in mice. CD-1 mice (10/sex/group) were exposed to the test substance as a vapor at concentrations of 0, 0.204, 0.135, or 0.065 mg/L for 8 hrs/day, for 5 consecutive days (nose-only). No POD. Dose dependent

changes in neurobehavioral examinations (square-box activity test, rota rod test, and hot plate test).

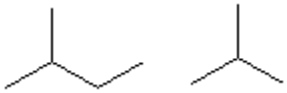
- OECD 411, OTS 870.3250, and OTS 798.2250: 90-day dermal study in rats. Sprague-Dawley rats (10/sex/group) had the test substance in mineral oil applied to the skin at doses of 0, 100, 300, or 600 mg/kg/day for 6 hrs/day, 5 days/wk for 13 weeks. There were no mortalities or clinical signs. Very slight to moderate erythema, very slight to slight edema, and/or scabbing were observed at the test site in treated animals; however, findings were also observed in vehicle control groups and were determined to be unrelated to treatment. No treatment related body weight changes or effects on food consumption observed. No ophthalmological findings, hematology findings, or clinical biochemistry findings. No changes to organ weights, gross findings, or histopathology findings. Mononuclear infiltrates in treated, untreated, and inguinal skin observed which were considered unrelated to treatment based on the lack of systemic microscopic findings and because findings were observed in controls as well. NOAEL = 600 mg/kg/day based on no adverse effects at the highest dose tested.
- Non-Guideline Study, comparable to OECD 410: 3-week dermal study in rabbits. New Zealand White rabbits (10/sex/group) had the neat test substance applied to the dorsal skin at concentrations of 0.2, 0.67, or 2 g/kg for 5 days/week for 3 weeks. Controls were untreated. Two female rabbits in the high-dose group died. One male in the high-dose group was sacrificed in moribund condition. Hair loss, hyperirritability, hindlimb paresis, and decreased motor activity were observed. Body weights at high-dose significantly lower at weeks 1-3, at mid-dose at weeks 2 and 3, and at low-dose at week 3. Cumulative body weight gain was significantly lower for all 3 weeks for the low-dose and mid-dose groups. Increased SGOT, globulin, and potassium and a significant decrease in albumin/globulin ratio observed for the high-dose group. Albumin and alkaline phosphatase levels were significantly decreased in the high-dose group. Alkaline phosphatase significantly decreased in the mid-dose group. Increased glucose levels in the mid- and high-dose groups relative to sham controls, and in the chloride levels of the high-dose group. Increased WBC counts in the mid-and high-dose groups. Significantly decreased erythrocyte levels in high-dose group. Hemoglobin levels were decreased at the mid- and high-dose compared to controls. Changes observed in differential leukocyte values (not specified). No POD established.
- Non-Guideline Study, comparable to OECD 410: 3-week dermal study in rabbits. New Zealand White rabbits (6-8/sex/group) had the neat test substance applied to the dorsal skin under occlusive conditions at concentrations of 0, 4, or 8 ml/kg/day. Animals were treated daily for 5 consecutive days followed by 2 days of rest and an additional 5 days of treatment. Mortality was observed at 8ml/kg/day (67%). Progressive deterioration at the test site was observed at both doses with skin becoming necrotic, appearing thickened, cracked or bloody. Test sites became odiferous and green. Body weight loss was observed in both treated groups. Necropsy revealed skin lesions, congested kidneys, and mottled livers of friable consistency at 4 ml/kg/day. At 8 ml/kg/day, anorexia, hemorrhagic mesenteric lymph nodes, abnormal kidneys and livers, friable

[redacted]

livers, and skin lesions were observed. Histopathology revealed slight to severe cutaneous lesions and multifocal necrosis (moderate to severe) in 2 animals at 8 ml/kg/day. Skin acanthosis, acute and chronic inflammation, crusting, congestion, dermal oedema, multifocal epidermal microabscesses, hyperkeratosis, epidermal necrolysis, and parakeratosis observed in both test groups. No POD selected.

- Non-Guideline Study, comparable to OECD 414: Prenatal inhalation developmental study in rats. Sprague-Dawley rats (20 dams/group) were exposed to the test substance as a vapor via whole body inhalation at concentrations of 0 (sham), 101.8, or 401.5 ppm for 6 hrs/day, on GD6-15. Maternal and Developmental NOAEC of 401.5 ppm (2110 mg/m3) based on no adverse effects.
- OECD 414 and OPPTS 870.3700: Prenatal dermal developmental study in rats. Sprague-Dawley rats (25 females/group) had the test substance in mineral oil applied to the skin at doses of 0 (sham and vehicle), 100, 300, or 600 mg/kg/day for 6 hrs/day on GD 0-19. No mortalities. Hair loss and colored material in the urogenital and ventral abdominal areas observed but unrelated to treatment based on similar frequencies across all groups; most likely a result of inability to groom. No changes to body weights, body weight gain, or gravid uterine weights. No effects on food consumption, behavior, organ weights, gross or histopathology findings. Three females in the 300 mg/kg/day group were nongravid (3 in sham control, 4 in vehicle control). No significant treatment related effects were observed on developmental parameters including pup body weights, number of live offspring, sex ratio, postnatal survival, litter size and weight, and external, skeletal, or visceral malformations. Maternal and Developmental NOAEL = 600 mg/kg/day.

F.2.13 Isobutane/2-methylbutane mixture (50:50 wt%), CASRN Not Available



Tier 3 Representative Isoparaffin

OECD SIDS **for Isopentane:**

- Test Guideline Not Specified: 90-day repeated dose inhalation toxicity study in rats. Fischer 344 rats (number/sex not specified) were exposed to 50/50 wt% 2-methylbutane/isobutane at a concentration of 0, 1000, or 4500 ppm (~ 3 and 13.5 mg/L) for 90 days, 5 days/week, 6 hours/day. Statistically significant increase in kidney pathology scores of males at 1000 ppm, however, control scores were considered to be unusually low, no significant findings in other groups. NOAEL = 4500 ppm (~13,500 mg/m3); NOAECadj = 2411 mg/m^3.

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F.2.14 Commercial hexane, CASRN Not Available

Structure not available

Tier 2 Analogous Mixture

U.S. EPA 2009 PPRTV:

Repeated-Dose Toxicity:

- **NOAECadj = 804 mg/m^3**, NOAEL =877 mg/m^3 and LOAEL=3510 mg/m^3, neuropathology, muscle atrophy, body weight reductions, and increased severity of chronic nephritis in male rats. Test substance consisted of n-hexane (50%), methylcyclopentane (~15%), 3-methylpentane (~15%), and 2-methylpentane (~15%) (rat inhalation 6 month study used to derive subchronic p-RfC (IRDC 1992a,b as cited in US EPA 2009 PPRTV).
- **LOAECadj = 564 mg/m^3** (lowest dose tested), nasal and laryngeal lesions. The test substance consisted of 51.5% *n*-hexane, 16% methylcyclopentane, 16.1% 3-methylpentane, 12.9% 2-methylpentane, 3.3% cyclohexane, and trace amounts of other hydrocarbons (rat inhalation 2-year study used to derive chronic p-RfC, Biodynamics 1993a and Daughtrey et al. 1999 as cited in USEPA 2009 PPRTV).

Developmental Toxicity:

- Developmental NOAEL = 3000 ppm and LOAEL = 9000 ppm based on skeletal variations (bilateral bone islands at the first lumbar arch, unossified intermediate phalanges). Test guideline not specified. Developmental toxicity study in mice. (PPRTV)
- Developmental NOAEC = 3000 ppm, LOAEL = 9000 ppm based on reduced body weights in F1 after PND 14 and F2 after PND 7. Two-generation reproductive/developmental study in rats (PPRTV)

Carcinogenicity:

- Screening-level provisional inhalation unit risk of 2E-4 per mg/m^3, based on combined incidence of pituitary adenomas and adenocarcinomas in female mice in 2 year inhalation study. In this study, 50 animals/sex/group were exposed 6 hours/day, 5 days/week, to a commercial hexane preparation at targeted inhalation concentrations of 0, 900, 3,000, or 9,000 ppm for 2 years. The test substance consisted of 51.5% *n*-hexane, 16% methylcyclopentane, 16.1% 3-methylpentane, 12.9% 2-methylpentane, 3.3% cyclohexane, and trace amounts of other hydrocarbons. When benign and malignant tumors were combined, the incidence reached statistical significance in the high-concentration group. There was also an increased incidence of pituitary adenomas and adenocarcinomas in exposed females. For these tumors there was a significantly elevated incidence at each exposure concentration. The inhalation unit risk is based on the combined incidence of pituitary adenomas and adenocarcinomas in female mice. (Biodynamics 1993b and Daughtrey et al. 1999 as cited in EPA 2009 PPRTV).

[redacted]

F.2.15 Stoddard Solvent IIC, CASRN 64742-88-7

Structure not available

Tier 2 Analogous Mixture

PPRTV for Midrange Aliphatic Hydrocarbon Streams (2009)

- NTP Protocol: Chronic inhalation carcinogenicity assay in F344 rats and B6C3F1 mice. Test material characterized as C10-13 n-paraffins, isoparaffins, and cycloparaffins with < 1.0% aromatics. 50 animals/sex/species were exposed to vapor concentrations of 0, 138 (male rats only), 550, 1100, or 2200 (male and female mice and female rats only) mg/m^3 for 6 hours/day, 5 days/week for 2 years. Cage-side observations were completely twice daily. Body weights and clinical signs of toxicity were recorded weekly through the first month, monthly until Week 89, and biweekly thereafter. Organ weights were not recorded at sacrifice. Comprehensive histopathological examinations were completed at sacrifice. Evaluation of the role of α_{2u}-globulin nephropathy was conducted.

- Rats: In rats, survival was significantly decreased in males at 138 and 1100 mg/m^3 and in females at 2200 mg/m^3. No treatment-related body weight changes or clinical signs were observed in rats. Male rats exhibited renal papillary mineralization at all concentrations and renal tubular hyperplasia and transitional epithelial hyperplasia of the renal pelvis at 550 and 1100 mg/m^3. Kidney effects were attributed to α_{2u}-globulin nephropathy; however, a mode-of-action analysis was not conducted and the endpoint is considered relevant to human health. Increased incidence of adrenal medullary hyperplasia in males at 550 mg/m^3 was considered adverse but insufficient information was available to determine whether the effect is a preneoplastic lesion, partially due to high background incidence in controls. Concentration-related increased incidence of adrenal pheochromocytomas was observed in males at 550 and 1100 mg/m^3. The NOAEC was 138 mg/m^3 and the LOAEC was 550 mg/m^3 based on adrenal medullary hyperplasia in male rats. "Some evidence of carcinogenic activity" was observed in males rats based on adrenal pheochromocytomas.

  Mice: In mice, survival was not affected by treatment. No treatment-related changes in body weights in males or clinical signs in males or females were observed. Mean body weights of exposed female mice at all concentrations were increased by 6-12% relative to controls. Increased incidence of basophilic and eosinophilic foci in the liver was observed in male mice at 1100 mg/m^3 and significantly increased incidence of eosinophilic foci in the liver was observed in female mice at 2200 mg/m^3. Significantly increased incidence of hepatocellular adenomas was observed in female mice; however, as incidence of liver tumors in this strain of mouse is affected by body weight, it was concluded that the increase in liver tumors was primarily due to the increased body weight in the exposed females. The NOAEC was 1100 mg/m^3 and the LOAEC was 2200 mg/m^3 based on eosinophilic foci in the liver in female mice. "Equivocal evidence of carcinogenicity" was observed in female mice based on hepatocellular adenomas.

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F.2.16 White mineral oils, CASRN Not Available

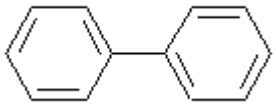
Structure Not Available

Tier 2 Analogous Mixture

PPRTV for White Mineral Oils (2009):

- Test Guideline Not Specified: White mineral oil has long been safely used for the treatment of constipation. A maintenance dose of 1–3 mL/kg-day (~870–2600 mg/kg-day) was recommended by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHN, 2006) or treatment of constipation in children >1 year of age. EPA (2009) selected the lower end of the therapeutic range (870 mg/kg-day) as a NOAEL for use in deriving a subchronic p-RfD of 30 mg/kg/day.

F.2.17 1,1-Biphenyl, CASRN 92-52-4



Analogue

8(e) Database

- Test Guideline Not Specified (Acute oral toxicity): LD50 (rat) = 2140 mg/kg-bw
- Test Guideline Not Specified (Dermal irritation): severe skin irritant
- Test Guideline Not Specified (Eye irritation): Mild eye irritant
- Test Guideline Not Specified (Repeated dose toxicity): Groups of 26 male and 26 female young adult rats were fed control or biphenyl-containing diets supplying 0, 300, 1000, and 2800 ppm biphenyl (~25, 75, and 215 mg biphenyl/kg/day, respectively, the nominal doses) for approximately ten weeks prior to breeding, and continuing through breeding (two weeks). An additional satellite group of P1 females (4/dose) was included primarily for assessments of kidney function in adult non-pregnant females during the pre-breeding period. The satellite female group was given biphenyl-containing diets concurrent with the P1 animals during pre-breeding. Satellite females were removed from study/terminated at the end of the pre-breeding period. After breeding, P1 males continued on the test diets for an additional 5-7 weeks (15-17 weeks total exposure). After breeding, P1 females continued on the test diets through gestation and lactation (16-18 weeks total exposure). F1 offspring were divided into Cohorts 1A, 1B, 2A, 2B and 3 at weaning (postnatal day (PND 21) as follows Cohort 1 A (22-24/sex/dose, 1 pup/sex/litter) were used to evaluate reproductive/endocrine toxicity to PND 90. Cohort 1 B (22-24/sex/dose, 1 pup/sex/litter) was used to generate a second generation of offspring. Cohort 1 B males and females had a total postnatal exposure of approximately 19 and 17 weeks, respectively. Cohort 2A (11-12/sex/dose, 1 pup/sex/litter) were used for developmental neurotoxicity assessments to PND 78. Cohort 2B (10/sex/dose, 1 pup/litter) were used to assess neuropathology on PND 22. Cohort 3 (10/sex/dose, 1 pup/litter) were used for developmental

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immunotoxicity to PND 56. Summary of effect Nominal dose levels (mg/kg/day) were achieved across both P1 and F1 generations; however, during some study intervals (e.g., PND 35-56), F1 offspring had greater biphenyl intake per kg body weight than P1 males and pre-breeding females. F1 offspring diets, which were adjusted to one-half normal concentrations from PND 21-35, returned to full concentration diets on PND 35; however, offspring continued to eat more diet/kg body weight, resulting in higher dose levels than the adults. Systemic toxicity was assessed across life stages. In the parental generation, high-dose biphenyl caused slight decreases in body weights and body weight gains, corresponding to decreased feed consumption in males and females throughout pre-breeding and continuing post-breeding for males and through the first week of gestation and then in the lactation period for P1 females. By PND 7, there was a treatment-related decrease in high-dose male and female F1 pup weights (6.8-8.2%) compared to the control group. This period of lactation (LD 0-7) corresponded with the period of highest test material intake by the P1 dams. In addition, the effects on pup weight were consistent with the lower maternal body weights on LD 1 (4.5%), 4 (5.2%), and 7 (6.4%) and sustained decreases in maternal feed consumption during the first week of lactation, which potentially lowered the ability of the dams to maintain offspring body weights. In the offspring Cohorts 1 A, 1 B, 2A and 3, body weights, body weight gains and feed consumption were decreased in the high dose group throughout the majority of the exposure period between PND 42 and the respective cohort termination. In Cohort 1 B P2 females, body weights were decreased throughout gestation by = 6.7% relative to controls with a corresponding decrease in GD 0-7 body weight gain of 17% and a slight decrease in feed consumption compared to controls. Cohort 1 B P2 lactation body weights, body weight gains and feed consumption were decreased during the first week of lactation, which subsequently increased during the last two weeks of lactation. There were no treatment-related effects on F2 pup body weights at < 2800 ppm biphenyl during lactation. Although high-dose pup body weights on PND 7 were decreased relative to controls in the F1 generation, the pup body weight effect was not reproduced in the F2 generation. There were no treatment-related changes in any of the hematology or clinical chemistry parameters in males or females at any dose level across the two generations. Urinalysis of non-pregnant satellite group females given 2800 ppm revealed the presence of treatment-related smooth ovoid crystals of various sizes (10-40 microns) and shapes in the urinary sediment. In Cohort 1 A females and Cohort 1 B P2 males given 2800 ppm, there was a treatment-related increase in urine volume and decrease in Specific gravity. Urinary sediments from Cohort 1 A males and females, and Cohort 1 B P2 males given 2800 ppm had treatment-related presence of amorphous phosphate crystals. Cohort 1 B P2 males and P2 females given 2800 ppm had treatment-related, higher severity of hematuria (blood in the urine) compared to controls. This biphenyl extended one-generation study identified kidney, urinary bladder and liver as target organs for biphenyl-induced toxicity.

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Treatment-related organ weight changes were confined to the liver and kidney in the P2 generation. Cohort 1 B P2 males and females given 2800 ppm had treatment related higher absolute and relative liver weights and Cohort 1 B P2 females given 2800 ppm had higher absolute and relative kidney weights compared to the control. With the exception of treatment-related gross findings of calculi in the urinary bladder and thickened bladder wall in 2 of 19 Cohort 1 B P2 males given 2800 ppm, there were no other gross pathological observations in any of the organs examined in males or females at any dose level across the two generations. Within the 2800 ppm group across the two generations, a small proportion of males had treatment related histopathological changes largely confined to the papilla, renal pelvic epithelium and/or the collecting ducts. Salient treatment-related changes include focal or multifocal hyperplasia of epithelium. Within the 2800 ppm group across the two generations, a small proportion of males had treatment-related histopathological changes largely confined to the papilla, renal pelvic epithelium and/or the collecting ducts. Salient treatment-related changes include local or multifocal hyperplasia of epithelium of the papilla and/or the renal pelvic epithelium, multifocal epithelial hyperplasia and hypertrophy of the collecting ducts, and multifocal subacute to chronic inflammation of the papilla and/or pelvic epithelium. The severity of most of these changes were very slight or slight or occasionally moderate. Other less frequent treatment-related changes variably noted between P1, Cohort 1 A and P2 males given 2800 ppm included slight multifocal necrosis of the collecting duct epithelium, slight local edema at the tip of the papilla, slight local ulceration of the papilla, and slight hemorrhage in the renal pelvis. A few of the high-dose males, particularly in the Cohort 1 A and P2 generations had treatment-related presence of an eosinophilic to red, fine granular to aggregated precipitated material in the renal pelvis admixed with red blood cells consistent with calculi likely urinary precipitates of the test material and/or its metabolites. The treatment-related changes in the kidney of males given 2800 ppm are consistent with chronic irritant effects of these urinary precipitates or calculi on the collecting ducts, renal pelvis and papilla. P1 females given 1000 or 2800 ppm had treatment related very slight or slight degeneration of tubules largely confined to the outer stripe of the outer medulla. The change was characterized by very slightly dilated tubular lumens at multiple loci, lined by epithelial cells that variably contained fine cytoplasmic vacuoles and were very slightly reduced in cell height (attenuated) compared to the controls. The lumens of these tubules often contained increased amounts of eosinophilic homogeneous or globular material compared to the controls. In addition, Cohort 1 A and P2 females given 2800 ppm had treatment-related increased incidence and severity of medullary tubular mineralization. Other treatment-related histopathologic changes noted in a small proportion of 2800 ppm P2 females included slight focal or multifocal hyperplasia of papillary epithelium and slight multifocal hyperplasia and hypertrophy of the epithelium of the collecting ducts in the papilla. The urinary bladder of P1, Cohort 1 A and P2 males and females

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given 2800 ppm had treatment-related, very slight or slight simple diffuse urothelial hyperplasia and a very slight multifocal subacute to chronic inflammation in the lamina propria underlying the urothelial lining of the bladder. The hyperplasia was characterized by uniform thickening of the urothelium (simple hyperplasia). These changes were consistent with chronic irritant effects on the urothelial lining of the bladder by urinary precipitates or calculi related to the test material. In the liver, P1 and Cohort 1 A males given 1000 or 2800 ppm, and P1 and Cohort 1 A females given 2800 ppm had very slight hypertrophy of centrilobular/midzonal hepatocytes with increased cytoplasmic eosinophilia. In the second generation, P2 males and females given 1000 or 2800 ppm had a very slight or slight treatment-related centrilobular/midzonal hypertrophy with increased cytoplasmic eosinophilia. The hepatocyte hypertrophy with increased cytoplasmic eosinophilia was interpreted to be a non-adverse adaptive change as a response to the continued ingestion of biphenyl.

- Females were dosed daily for two weeks prior to breeding, through breeding (up to two weeks), gestation (three weeks), lactation (three weeks) and until necropsy on post-partum days 22-24. The males were dosed for two weeks prior to breeding, through breeding (up to two weeks), and until necropsy (test day 36). Dietary administration of 5500 ppm biphenyl to Crl:CD(SD) rats resulted in treatment-related decreases in body weight and/or body weight gains in males and females throughout the study, including premating, gestation and lactation phases in the females. Decreases in gestation body weight gains reached 19.5% on GD 14-21 and 13% throughout gestation (GD 0-21). Lactation body weights were decreased from the onset of lactation, reaching a 14.5% decrease on LD 7, but body weights gradually increased thereafter to levels similar to controls on LD 21. At 2750 ppm, premating body weights in dams were decreased when treatment was initiated, but returned to values similar to control dams thereafter. At both 2750 and 5500 ppm biphenyl, decreases in body weights/gains corresponded with decreases in feed consumption. There were no treatment-related effects on body weights in the 1375 ppm group. High-dose pups had treatment-related decreases in body weights on PND 7, which corresponded with maximum decreases in lactation body weight and feed consumption in maternal animals; body weights in these pups were similar to controls by PND 21. Pup body weights in the 2750 ppm group showed a similar pattern of effect to high-dose pups with maximal decreases in pup body weight on PND 7 and recovery throughout the remainder of the lactation period, Pup body weights were not affected in the 1375 ppm group. Absolute and relative liver weights were increased in males and females given 2750 or 5500 ppm biphenyl. Relative kidney weights also were increased in high-dose males and females, as well as males in the 2750 ppm group. Histopathologically, biphenyl treatment at 2750 and 5500 ppm resulted in very slight-to-slight hypertrophy of midzonal/centrilobular hepatocytes with increased eosinophilia in both males and females. Kidneys in high-dose males and females exhibited multiple histopathological changes, including

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dilatation of the tubules, necrosis of the tubular epithelium and papilla with regenerative hyperplasia, hyperplasia of the pelvic epithelium, and interstitial inflammation. Most of these findings were graded very slight-to slight. Treatment-related kidney findings at 2750 ppm generally included some of the same changes seen in high-dose animals (e.g., tubular dilatation, inflammation, and hyperplasia), but generally at a lesser severity and Iower incidence. These kidney histopathological findings were consistent with possible biphenyl-induced crystalluria (precipitation of parent biphenyl or its metabolite in the urine filtrate), possibly causing a partial obstruction to urine outflow. ln addition, females at all dose levels had very slight-to-slight bilateral tubular degeneration Iocalized to the outer stripe of the outer medulla, a finding that was not seen in males. The significance of this finding is unclear

Genotox

- Test Guideline Not Specified (Gene mutation): Negative in Salmonella with and without activation
- Test Guideline Not Specified (Gene mutation): Positive with activation and negative without activation in mouse lymphoma
- Test Guideline Not Specified (Sister chromatid exchanges): positive in vitro in mammalian nonhuman with dose response
- Test Guideline Not Specified (Unscheduled DNA synthesis): Negative in human fibroblast and rat primary hepatocytes in vitro

RTECS

- Test Guideline Not Specified (Acute intravenous toxicity): LD50 (mouse) 56 mg/kg-bw
- Test Guideline Not Specified (Acute oral toxicity): LD50 (mouse) = 1900 mg/kg-bw. Clinical signs include somnolence (general depressed activity)
- Test Guideline Not Specified (Acute oral toxicity): LD50 (rat) 2140 mg/kg-bw. Clinical signs include somnolence (general depressed activity), muscle weakness.
- Test Guideline Not Specified (Acute oral toxicity): LD50 (rabbit) 2400 mg/kg-bw
- Test Guideline Not Specified (Acute dermal toxicity): LD50 (rabbit) > 5010 mg/kg-bw

TSCATS

- Test Guideline Not Specified (Acute oral toxicity): LD50 (rat) = 3.28 g/kg-bw.
- Test Guideline Not Specified (Acute oral toxicity): LD50 (rat) = 2.400 g/kg-bw. Clinical signs observed include reduced appetite and activity, increasing weakness, ocular discharge, collapse and death.
- Test Guideline Not Specified (Acute oral toxicity): LD50 (rat) > 3.98 g/kg-bw.
- Test Guideline Not Specified (Acute inhalation toxicity): LD50 (rat) = 2.18 g/kg-bw. Clinical observations included sluggishness, prostration, and narcosis.

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- Test Guideline Not Specified (Acute dermal toxicity): LD50 (rabbit) = 2.50 g/kg-bw
- Test Guideline Not Specified (Acute dermal toxicity): LD50 (rabbit) > 5.010 g/kg-bw. Clinical signs included reduced appetite and activity, increasing weakness, collapse and death.
- Test Guideline Not Specified (Acute dermal toxicity): No mortalities observed in rabbits at 2.0 or 3.98 g/kg-bw
- Test Guideline Not Specified (Ames test): Negative in Salmonella with and without activation
- Test Guideline Not Specified (Unscheduled DNA Synthesis assay): No significant increase in unscheduled DNA synthesis in rat hepatocytes

EPA IRIS (2013)

Non-cancer:

Critical oral study selected by EPA IRIS:

- Test guideline not specified: 2-year dietary study in rats: $BMDL_{10HED}$ = 13.9 mg/kg/d based on renal papillary mineralization in male rats. Umeda et al. (2002) exposed F344 rats (50/sex/group) to biphenyl in the diet for 2 years at concentrations of 0, 500, 1,500, or 4,500 ppm (corresponding to doses of 36.4, 110, and 378 mg/kg-day, respectively, for males, and 42.7, 128, and 438 mg/kg-day, respectively, for females). Mean body weights of 4,500 ppm male and female rats were lower than those of controls throughout most of the study period and were approximately 20% lower than respective controls at terminal sacrifice. There was no statistically significant effect on mean body weights of 500 or 1,500 ppm males or females. Survival of low- and mid-dose male and female rats was reported not to differ statistically significantly from controls.

  The study authors reported that 3/50 of the 4,500 ppm female rats died after 13–26 weeks of biphenyl exposure and attributed the deaths to marked mineralization of the kidneys and heart. However, they also indicated that survival of this group was not adversely affected thereafter. Significantly decreased survival was noted only for the group of 4,500 ppm male rats, 19/50 of which died prior to terminal sacrifice. The first death occurred around treatment week 36; this rat exhibited urinary bladder calculi. Survival data for the other groups were not provided. Evidence of hematuria (blood in the urine) was first noted in 4,500 ppm male rats around week 40 and was observed in a total of 32/50 of the 4,500 ppm males during the remainder of the treatment period; 14 of these rats appeared anemic. Hematuria and bladder tumors were considered as primary causes of death among the 4,500 ppm males (n = 19) that died prior to terminal sacrifice.

  Urinalysis performed during the final treatment week revealed statistically significantly increased urinary pH in the 31 remaining 4,500 ppm male rats (pH of 7.97 versus 7.66 for controls; $p < 0.05$), with occult blood noted in the urine of 23 of

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these males. Urine samples in 10/37 surviving 4,500 ppm females tested positive for occult blood. Relative kidney weights of 1,500 and 4,500 ppm males and females and absolute kidney weights of 4,500 ppm males were statistically significantly increased (actual data were not reported).

Gross pathologic examinations at premature death or terminal sacrifice revealed the presence of calculi in the bladder of 43/50 of the 4,500 ppm males and 8/50 of the 4,500 ppm females, but not in the other dose groups. It was noted that 30/32 of the 4,500 ppm male rats with hematuria also exhibited kidney or urinary bladder calculi.

Histopathological lesions of the ureter, kidney, and urinary bladder associated with biphenyl exposure were reported in male and female rats. The incidences of transitional cell hyperplasia and dilatation in the ureter were increased in the 4,500-ppm rats compared to controls. In the renal pelvis, incidences of hyperplasia and mineralization showed dose-related increases in males and females; the incidence of desquamation and calculi were increased primarily in male rats. Other treatment-related lesions in the kidney of male and female rats included mineralization of the corticomedullary junction and mineralization of the papilla; treatment-related increases in the incidence of papillary necrosis, infarct, and hemosiderin deposition in the kidney occurred predominantly in exposed females. In the urinary bladder, nonneoplastic lesions were found predominantly in male rats, and included transitional cell hyperplasia, squamous cell metaplasia and hyperplasia, inflammatory polyps, and calculi. An increased incidence of tumors associated with biphenyl administration was limited to tumors of the urinary bladder in male rats (see Section II.A).

In summary, this study identified a NOAEL of 500 ppm (42.7 mg/kg-day) and a lowest-observed-adverse-effect level (LOAEL) of 1,500 ppm (128 mg/kg-day) for nonneoplastic kidney lesions (simple transitional cell hyperplasia in the renal pelvis and hemosiderin deposits) in female F344 rats exposed to biphenyl in the diet for 2 years.

EPA calculated a $BMDL_{10HED}$ = 13.9 mg/kg-day based on renal papillary mineralization in male F344 rats in the 2-year dietary study (Umeda et al. 2002).

*Conversion Factors and Assumptions — Rats in the principal study were exposed continuously via diet; therefore, no adjustment for intermittent dosing was required. BMDL10/HED = 95% lower confidence limit on the maximum likelihood estimate of the dose corresponding to a 10% extra risk, and expressed as a human equivalent dose (HED) using BW3/4 scaling (U.S. EPA, 2011).

Inhalation: No critical study was selected by EPA IRIS:

[redacted]

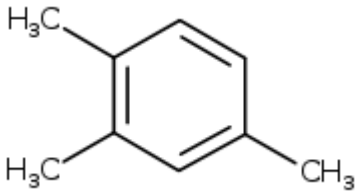
- No inhalation RfC was derived due to the lack of inhalation studies of biphenyl toxicity following chronic exposure and studies involving subchronic exposure that were inadequate for RfC derivation. Repeated exposure of mice to biphenyl vapors for 13 weeks resulted in high incidences of pneumonia and tracheal hyperplasia, and high incidences of congestion and edema in the lungs, liver, and kidney (Sun, 1977); however, study limitations and lack of supporting data preclude the use of this study for deriving an RfC for biphenyl. Study limitations include highly variable biphenyl exposure concentrations during the first half of the study, high mortality after 46 exposures in one group of biphenyl-exposed mice due to an overheating event and cannibalization that necessitated the use of replacement animals, and limitations in the reporting of histopathological findings.

Cancer:

- Under EPA's Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005a), the database for biphenyl provides "suggestive evidence of carcinogenic potential" based on increased incidence of urinary bladder tumors (transitional cell papillomas and carcinomas) in male F344 rats (Umeda et al., 2002) and liver tumors (hepatocellular adenomas and carcinomas) in female BDF1 mice (Umeda et al., 2005) exposed to biphenyl in the diet for 104 weeks, as well as information on mode of carcinogenic action. The carcinogenic potential of biphenyl in humans has not been investigated.

  Based on a 2-year dietary study in BDF1 mice (Umeda et al. 2005), EPA derived a cancer oral slope factor= 8.2×10^{-3} $(mg/kg\text{-}day)^{-1}$ based on liver tumors (adenomas or carcinomas) in females.

F.2.18 1,2,4-Trimethylbenzene, CASRN 95-63-6



Tier 3 Representative Aromatic

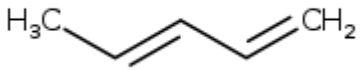
IRIS Toxicological Review of Trimethylbenzenes (2016):

- Test Guideline Not Specified: 3-month subchronic inhalation toxicity study in rats. Rats (unspecified strain and number) were exposed to the test substance at concentrations of 0, 25, 100, or 250 ppm (0, 123, 491, 1227 mg/m^3) for 6 hrs/day, 5 days/week, for 3 months. No body weight effects or clinical signs of toxicity. Decrease in pain-sensitivity in concentration-related manner. At 1227 mg/m^3, significantly increased failure in rotarod performance test (40% failure) after 8 or 13 weeks. After recovery, failure was not significant but still increased (30%) and decrease in pain sensitivity was no longer

[redacted]

significantly different compared to controls. NOAEL = 123 mg/m^3 and LOAEL = 491 mg/m_3 based on significantly decreased pain sensitivity; BMCL = 25.1 mg/m^3 and BMDL = 3.5 mg/kg/day after route-to-route extrapolation. (Korsak and Rydzynski 1996)

F.2.19 1,3-Pentadiene, CASRN 504-60-9



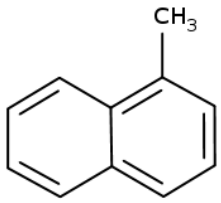
Tier 3 Representative Olefin

OECD SIDS:

- OECD 401: LD50 (rat) < 5000 mg/kg
- OECD 403: LC50 (rats) > 20917 ppm (58.2 mg/L)
- OECD 403: LC50 (mice) > 20917 ppm (58.2 mg/L)
- OECD 402: LD50 (rabbit) > 3.2 g/kg
- Test Guideline Not Specified: Moderately irritating to rabbit skin
- OECD 471: Negative in S. typhimurium with and without activation
- OECD 474: Negative in mice via inhalation up to 300 ppm (0.834 mg/L)
- OECD 474: Negative in rats via inhalation up to 7000 ppm (19.5 mg/L)
- Test Guideline Not Specified: Subchronic oral study in rats. Rats (strain, sex, and number) were administered the test substance (dose and duration not provided). There was no evidence of neurotoxicity. No additional information provided.
- Test Guideline Not Specified: 2-day inhalation study in mice (dose selection study for micronucleus study). Mice (2/sex) were exposed to target concentrations of 0, 100, 500 and 2000 ppm (equivalent to 0, 0.278, 1.39 and 5.56 mg/L) 6 hours/day for 2 days. All mice died in the 500 and 2000 ppm groups. All mice survived in the 100 ppm group. No additional information is provided.
- OECD 422: Sprague Dawley rats (number not specified) were administered the test substance at doses of 30, 100, and 1000 mg/kg/day prior to mating, during mating, and post-mating. There were transient decreases in food consumption at 1000 mg/kg/day. There were no systemic effects observed based on gross and microscopic evaluations of organs. There was no evidence of reproductive toxicity. NOEL (maternal animals) = 100 mg/kg/day. NOEL = 1000 mg/kg/day (highest dose tested) for P and F1 generations. No additional information provided.

[redacted]

F.2.20 1-Methylnaphthalene, CASRN 90-12-0



Tier 3 Representative Aromatic

PPRTV (2008)

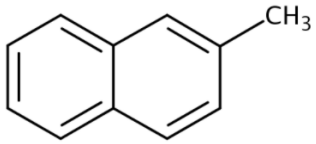
- Test Guideline Not Specified: 13-week pilot dietary study in mice. B6C3F1 mice (10/sex/group) were administered the test substance in the diet at concentrations of 0, 0.0163, 0.049, 0.147, 0.44, or 1.33% for 13 weeks. In the 0.44 and 1.33% groups, mice exhibited growth retardation that was attributed to refusal to eat. No histopathological changes were observed (the extent of histopathological assessment was not described). No POD selected.
- TGNS: 81-week repeated dose chronic toxicity and carcinogenicity study in rats. B6C3F1 mice (50/sex/group) were administered the test substance in the diet at concentrations of 0, 0.075, or 0.15% (~71.6 and 140.2 mg/kg/day) for 81 weeks. Males had significantly (6-8%) increased absolute and relative brain and heart weights. In females, significantly decreased (17%) absolute and relative salivary gland weight, increased (7%) absolute heart weight, and decreased (35%) absolute and relative thymus weights were observed; thymus weight changes were related to the development of lymphoma in treated females. No changes were supported by any histopathological changes and statistics were restricted to simple t-tests; therefore, these findings were discounted for defining the LOAEL. Significant increased incidences of pulmonary alveolar proteinosis (PAP) were observed in treated mice (control – 8.2% in males, 10% in females). This was characterized as an accumulation of phospholipids in the alveolar lumens and appeared grossly as white protuberant nodules and histologically as visible filling of alveolar lumens with cholesterol crystals, foamy cells, and an amorphous acidophilic material. Alveolar walls and epithelial cells were generally intact; no evidence of prominent edema, alveolitis, lipidosis, or fibrosis. Significantly increased incidences of lung adenoma and combined adenoma or adenocarcinoma in males. A dose-related increased in elevated monocyte concentrations was observed, possibly as a response to the PAP. LOAEL = 71.6 mg/kg/day and PPRTV chronic screening value RfD = 7E-3 mg/kg/day (UF=1000) based on significantly increased incidences of pulmonary alveolar proteinosis. **PPRTV Oral Slope Factor** = 2.9E-2 $(mg/kg\text{-}day)^{-1}$. **ATSDR Oral MRL** = 0.07 mg/kg-day based on a LOAEL of 71.6 mg/kg-day for pulmonary alveolar proteinosis in female mice. **ATSDR CEL** = 71.6 mg/kg/day based on increased incidence of lung adenomas in males. (Murata et al. 1993)

[redacted]

Published Literature

- Test Guideline Not Specified: 13-week repeated dose inhalation toxicity study in F344 rats (10/sex/group) at concentrations of 0, 0.52, 4.08, or 30.83 ppm (corresponding to 0, 3.0, 23.7, or 179.3 mg/m^3) for 6 hr/day, 5 days/week. No adverse effects on body weights were observed. In males and females at the high concentration, prothrombin time was significantly increased. In males at the high concentration, APTT was significantly increased, serum ALT was significantly decreased, and serum albumin and sodium were significantly increased. These changes in hematological parameters were considered not to be adverse due to the small magnitude of change and no evidence of hemorrhage or coagulopathy. Bronchoalveolar lavage cell differentials and levels of LDH were not affected. Organ weights were not affected. Concentration-dependent mucous cell hyperplasia of the nasopharyngeal tissues was observed in males of all treatment groups and in females of the mid- and high-concentration groups. Transitional cell hyperplasia of the nasopharyngeal tissue was noted for males of the mid- and high-concentration groups. LOAEC = 0.52 ppm (3.0 mg/m^3) based on portal-of-entry (inhalation) effects. (Kim et al. 2020 Toxicol Res 36:13)

F.2.21 2-Methylnaphthalene, CASRN 91-57-6



Tier 3 Representative Aromatic

OECD SIDS:

- Test Guideline Not Specified: LD50 (rats) = 4050 mg/kg; shaggy fur, hunchbacked posture, pallor of the extremities, increased lacrimation, muscle tremors, diarrhea, lethargy and ataxia
- Test Guideline Not Specified: RD50 (rats/mice) = 67 mg/m^3
- OECD 402: LD50 (rats) > 2000 mg/kg
- OECD 473: Negative in Chinese hamster lung cells with and without metabolic activation
- Test Guideline Not Specified: Negative for Chromosomal aberrations and sister-chromatid exchange with and without metabolic activation
- Test Guideline Not Specified: 81-week dietary study in mice. B6C3F1 mice (10/sex/group) were administered the test substance (97%) in the diet at concentrations of 0, 0.075, or 0.15% for 81 weeks. SIDS states no carcinogenic potential; however, significantly increased incidence of total lung adenomas plus adenocarcinomas but not tumors observed. Incidences for lung adenomas or carcinomas in males were 2/49, 10/49, and 6/49. In females 5/50, 4/49, and 6/48. IRIS, ATSDR state inadequate information for carcinogenicity evaluation.

PPRTV:

- Test Guideline Not Specified: 81-week dietary study in mice. B6C3F1 mice (10/sex/group) were administered the test substance (97%) in the diet at concentrations of 0, 0.075, or 0.15% for 81 weeks. Systemic LOAEL = 0.075% (equivalent to 54.3 in

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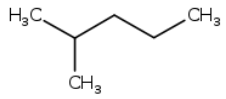
males and 50.3 in females) based on significant decreases in body weight in males and increased incidence of pulmonary alveolar proteinosis in both sexes. Reproductive NOAEL = 0.15% (equivalent to 113.8 in males and 107.6 in females) based on no reproductive effects at the highest dose tested. **Selected for Oral RfD in IRIS: RfD = 4E-3 mg/kg/day derived from $BMDL_{05}$ of 3.5 mg/kg/day and UF of 1000. PPRTV selected this value as the Subchronic p-RfD. ATSDR derived chronic oral MRL of 0.04 mg/kg/day using a UF of 100**

- Test Guideline Not Specified: 13-week Subchronic toxicity study in mice. B6C3F1 mice (10/sex/group) were administered the test substance in the diet at concentrations of 0, 0.0163, 0.049, 0.147, 0.44, or 1.33% for 13 weeks. Estimated doses were: 0, 29.4, 88.4, 265, 794, or 2400 mg/kg-day for males and 0, 31.8, 95.6, 287, 859, or 2600 mg/kg-day for females. NOAEL = 2500 mg/kg/day for both sexes. The growth retardation and reduced food consumption observed were considered non-adverse due to a lack of accompanying effects.

NTP**:**

- NTP Protocol: Ames Assay. Negative in Salmonella with and without metabolic activation

F.2.22 2-Methylpentane, CASRN 107-83-5



Tier 3 Representative Isoparaffin

ECHA Database and published literature:

Repeated-Dose Toxicity:

- **$LOAEL_{adj}$ = 1000 mg/kg/day** (only dose tested), reduced mixed nerve conduction velocities. Non-guideline study. Male Wistar rats (5−7/group) were administered 2-methylpentane by gavage in olive oil daily for 8 weeks. The exposure regimen consisted of administration of 0.4 mL solvent and 0.6 mL olive oil for the first 4 weeks, 0.6 mL solvent and 0.4 mL olive oil for a subsequent 2 weeks and 1.2 mL solvent and 0.8 mL olive oil for the final 2 weeks, for a time-weighted average dose of 1000 mg/kg/day. Body weight was measured every 2 weeks. Peripheral nerve activity was measured at the start of the experiment and every 2 weeks until termination. Histopathology examinations were not made. There was no change among the groups in the rates of body-weight gain throughout the experiment (Ono et al., 1981). There were slight but statistically significant ($p<0.05$) reductions in distal and proximal mixed nerve conduction velocities of animals receiving 2-methylpentane. (Ono et al. 1981. Int Arch Occup Environ Health 48:289; ECHA)
- **LOAECadj = 1420 mg/m^3**, decreased body weight gain. Non-guideline study: 14-week inhalation study in male Sprague-Dawley rats (number not reported) at a concentration of 1500 ppm (5300 mg/m^3) for 9 hrs/day, 5 days/week for 14 weeks. Endpoints were limited to body weight and neurotoxicity (neuromuscular function

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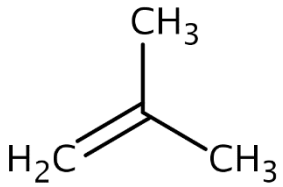
and nerve histology).LOEL < 1500 ppm (5300 mg/m^3) based on decreased body weight gain. LOAECadj = 1420 mg/m^3. (ECHA; Frontali et al. 1981. Clin Toxicol 18(12):1357).

F.2.23 2-Methylpropene, CASRN 115-11-7



Tier 3 Representative Olefin

OECD SIDS:

- Test Guideline Not Specified: LC50 (2-hr)(mice) = 180000 ppm (415 mg/L)
- Test Guideline Not Specified: LC50 (4-hr)(rats) = 270,000 ppm (620 mg/L)
- Test Guideline Not Specified: Ames Assay. Negative in Salmonella and E. coli with and without metabolic activation
- Test Guideline Not Specified: Cell Transformation Assay. Negative in vitro
- Test Guideline Not Specified: Mouse Lymphoma Assay. Negative in L5178Y cells with and without metabolic activation
- Test Guideline Not Specified: Micronucleus Assay. Negative in mice
- Test Guideline Not Specified: 28-day repeated dose study in rats. Sprague-Dawley rats (5/sex/group) were administered the test substance via oral gavage at doses of 1.5, 15, or 150 mg/kg/day. No mortalities. There were no changes to body weight or food consumption. Decreased white blood cell counts in the high-dose group observed (44% females, 11% males) but were within historical ranges. Slight, non-significant increases in BUN in males and blood glucose in females were observed but these were determined to be within the normal range of variation for this strain. NOAEL = 150 mg/kg/day based on no toxicologically significant effects at the highest dose tested.
- Test Guideline Not Specified: 13-week repeated dose study in rats. Sprague-Dawley rats (10/sex/group) were exposed via inhalation to the test substance at concentrations of 0, 250, 1000, or 8000 ppm (0.57, 2.29, 18.4 mg/L) for 6 hrs/day, 5 days/week, for 13 weeks. Increased urinary ketone bodies observed although this was of unknown significance. There were no histopathology findings. NOAEL = 8000 ppm (18.4 mg/L).
- NTP Protocol: 14-week repeated dose study in rats. F344/N rats (10/sex/group) were exposed to the test substance via inhalation at concentrations of 0, 500, 1000, 2000, 4000, 8000 ppm (1.14, 2.29, 4.59, 9.18, 18.4 mg/L) for 6 hrs/day, 5 days/week, for 14 weeks. No mortalities. No treatment related body weight changes, clinical signs, effects on hematology, or clinical chemistry findings. No effects on reproductive organs. Minimal nasal effects (hypertrophy of goblet cells in the nasopharyngeal duct) observed at 500 ppm and higher in both sexes. Increased liver weights in females at 1000 ppm and higher, however no concentration related changes observed. Increased kidney weights in males at 4000 ppm and higher; however, these effects did not exceed 10%.

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Significant increase in left epididymis weights and significant decrease in epididymal sperm motility in the 8000 ppm group. No significant differences in testes weights compared to controls. Time spent in estrus increased with a decrease in time spent in diestrus in treated females. No effects on reproductive organs. NOAEL = 8000 ppm (18.4 mg/L).

- NTP Protocol: 14-week repeated dose study in mice. B6C3F1 mice (10/sex/group) were exposed to the test substance via inhalation at concentrations of 0, 500, 1000, 2000, 4000, 8000 ppm (1.14, 2.29, 4.59, 9.18, 18.4 mg/L) for 6 hrs/day, 5 days/week, for 14 weeks. No mortalities. No treatment related body weight changes, clinical signs, effects on hematology, or clinical chemistry findings. No effects on reproductive organs. Increased kidney weights were observed in males in the 8000 ppm group and in females at 500 ppm and higher. Findings were not exposure concentration related. No histopathology findings observed. No effects on reproductive parameters or organs. NOAEL = 8000 ppm (18.4 mg/L).
- OECD 414: Prenatal Developmental study in rats. Wistar rats (24 mated females/group) were exposed to the test substance via inhalation (whole-body exposure) at target concentrations of 0, 500, 2000, or 8000 ppm (~1140, 4590, and 18400 mg/m3) for 6 hrs/day on GD 5-21. No maternal effects observed. No effects on the number, growth, or survival of fetuses in utero. No effect on fetal development. Major skeletal defects such as cleft sternal cartilage and xiphoid cartilage were observed in 3 (2), 5 (5), 5 (3), and 3 (3) fetuses (litters) in the control, 500, 2000, and 8000 ppm groups. Cleft sternebrae incidences were small and not dose related. No effects on the percentage of fetuses with minor external/visceral defects. Statistical, significant increase in the percentage and proportion of fetuses with external/visceral variants in the 8000 ppm group. This was due to the increased incidence of fetuses with the umbilical artery positioned on the left side of the bladder. Because this finding is variable in the strain (8.1-18.2% historical control) it was considered to be a chance finding and unrelated to treatment. Therefore, there were no adverse effects on fetuses. NOAEC = 18.4 mg/L based on no adverse effects at the highest dose tested.
- NTP Protocol: 105-week carcinogenicity study in rats. F344/N rats (50/sex/group) were exposed to the test substance via inhalation at concentrations of 0, 500, 2000, or 8000 ppm (1.14, 4.59, 18.4 mg/L) for 6 hrs/day, 5 days/week, for 105 weeks. Survival and mean body weights were comparable to controls. No clinical findings were observed. Increased incidence of thyroid gland follicular cell carcinoma in 8000 ppm male rats; however, no incidence of hyperplasia or adenoma were observed in males and no proliferative lesions were observed in these tissues in females. Minimal nasal effects (hyaline degeneration of the olfactory epithelium) observed at 500 ppm and higher in both sexes. These findings were considered to be a nonspecific adaptive response to inhalation of an irritating material. No nasal neoplasms were observed. Increased kidney weights were observed in males in the 8000 ppm group and in females at 500 ppm and higher. NOAEL = 2000 ppm (4.59 mg/L). Based on the incidence of follicular cell

carcinoma of the thyroid gland, there was some evidence of carcinogenic activity in male rats. There was no evidence of carcinogenicity in female rats.

- NTP Protocol: 105-week carcinogenicity study in mice. B6C3F1 mice (50/sex/group) were exposed to the test substance via inhalation at concentrations of 0, 500, 2000, or 8000 ppm (1.14, 4.59, 18.4 mg/L) for 6 hrs/day, 5 days/week, for 105 weeks. Survival and mean body weights were comparable to controls; however, slightly decreased body weight was observed in females at 2000 ppm and higher. No clinical findings were observed. Minimal nasal effects (hyaline degeneration of the olfactory epithelium) observed at 500 ppm and higher in both sexes and increased in incidence with exposure levels. Effects in males were significant. No nasal neoplasms were observed. Increased kidney weights were observed in males in the 8000 ppm group and in females at 500 ppm and higher. There was no evidence of carcinogenicity in mice.

NTP

- NTP Protocol: Micronucleus Assay. Negative in mice
- NTP Protocol: Ames Assay. Negative in Salmonella with and without metabolic activation

F.2.24 Benzene, CASRN 71-43-2

Tier 3 Representative Aromatic

EPA IRIS Toxicological Review of Benzene (Non-cancer Effects) (2002):

- Test Guideline Not Specified: Male Charles River CD-1 mice (5/group, 6-7 weeks of age) were exposed to 0, 31, 166, or 790 mg/L (0, 8, 40, or 180 mg/kg/day) benzene in drinking water for 28 days (Hsieh et al. 1988b). The treatment had no adverse effects with respect to mortality, clinical signs, body weight change, liver weight, or gross necropsy. A dose-related decrease in relative spleen weight was observed, significant at the high-exposure level. In one test, spleen cellularity was reported to be significantly decreased at all exposure levels, and in a separate test only at the high-exposure level. Although relative thymus weights were decreased at all exposure levels, the values were not statistically significantly different from control values. Dose-related hematological effects (erythrocytopenia, leukocytopenia, lymphocytopenia, increased MCV) were observed at all exposure levels. The authors indicated that the increased MCV and decreased HCT and numbers of RBCs were indicative of severe macrocytic anemia. Biphasic responses were observed in immunological tests, including mitogen-stimulated splenic lymphocyte proliferation; mixed splenic lymphocyte culture response to allogenic yeast artificial chromosome [YAC]-1 cells; cytotoxic splenic T lymphocyte response to allogenic YAC-1 cells with a significantly increased response at the low-exposure level; and significantly decreased responses at the mid- and/or high-exposure level. Using several methods to determine primary antibody response to SRBC, significantly decreased responsiveness was observed at the mid- and/or high-exposure levels. This response was either significantly increased or not different from controls in

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mice at the low-exposure level. This study identified a LOAEL of 8 mg/kg/day (the lowest dose tested) for hematologic and immunological effects in male mice exposed to benzene in drinking water for 30 days. No NOAEL was established. BMD modeling yielded a BMD of 2.2 mg/kg/day and a BMDL of 1.4 mg/kg/day.

- Test Guideline Not Specified: Female B6C3F1 mice (12/group, 6-7 weeks of age) were exposed to benzene in drinking water (containing emulphor to increase solubility of benzene) at levels of 0, 50, 1000, or 2000 mg/L (0, 12, 195, or 350 mg/kg/day, as calculated by the authors) for 30 days (White et al., 1984). Body weight was significantly decreased at the high-exposure level. A dose-related decrease in absolute and relative spleen weight was observed. In one test, spleen cellularity was reported to be significantly decreased at all exposure levels. Dose-related leukopenia and lymphocytopenia were observed. A dose-related decrease in eosinophils was observed. At the high-exposure level, significant decreases in levels of erythrocytes and hemoglobin were observed. No exposure-related effects were observed for levels of BUN, serum creatinine, SGOT, or SGPT, indicators of renal and hepatic damage. Dose-related changes were observed in immunological tests on spleen cells and in assays of bone marrow; decreases were observed with respect to IgM antibody forming cells/spleen in response to SRBC, lymphocyte proliferation response to the T cell mitogen Con A and the B cell mitogen LPS, number of T lymphocytes, and femoral GM-CFU; and an increase was observed in bone marrow cell DNA synthesis. These effects were not significant at 12 mg/kg/day but were dose-related. Of all the immunological indices tested, only one endpoint (stimulation index for lymphocyte proliferation of spleen cells in response to medium containing 05 µg/mL Con A) was significantly decreased at 12 mg/kg/day. The number of B lymphocytes was not affected, but the investigators commented that the number of B lymphocytes in the controls was lower than for historical controls for their laboratory. This study identifies a NOAEL of 12 mg/kg/day and a LOAEL of 195 mg/kg/day for hematologic effects in mice exposed to benzene in drinking water for 30 days and a LOAEL of 12 mg/kg/day for immunological effects. BMD modeling yielded a BMD of 11.6 mg/kg/day and a BMDL of 5.3 mg/kg/day.
- Test Guideline Not Specified: Occupational exposure. In a cross-sectional study, 44 workers (21 females, 23 males) were exposed to benzene for an average of 6.3 years (range: 0.7-16 years) at a median 8-hr TWA concentration of 31 ppm (99 mg/m^3). Exposed workers were subdivided into 2 groups of 22 – those exposed to greater than 99 mg/m^3 and those exposed to less than 99 mg/m^3. For the low and high exposure groups, the median 8-hr TWA concentration was 13.6 ppm (43.4 mg/m^3) and 91.9 ppm (294 mg/m^3), respectively. There were significant decreases in absolute lymphocyte count (ALC), WBC count, RBC count, hematocrit, and platelets and a significant increase in MCV in the high exposure group compared to controls, with ALC being the most sensitive endpoint and the only change at the 13.6 (43.4 mg/m^3) level; therefore, the LOAEC was 43.4 mg/m^3. BMD modeling of the ALC data yielded a $BMCL_{ADJ}$ of 8.2 mg/m^3. A BMDL of 1.2 mg/kg/day was derived using route-to-route extrapolation. An RfD of 4.0E-3 mg/kg/day was calculated (Rothman et al. 1996a).

EPA IRIS Chemical Assessment Summary for Benzene (2000):

- Known human carcinogen for all routes of exposure (Category A)

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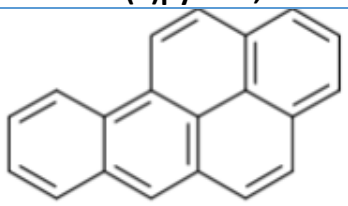
- Oral slope factor: 1.5E-2 to 5.5E-2 per (mg/kg)/day
- Drinking water unit risk: 4.4E-7 to 1.6E-6 per (µg/L)
- Inhalation unit risk: 2.2E-6 to 7.8E-6 per µg/m^3

  Infante et al. (1977b), in a retrospective cohort mortality study, examined the leukemogenic effects of benzene exposure in 748 white male workers exposed at least 1 day while employed in the manufacture of rubber products. Exposure occurred from 1940 to 1949 and vital status was obtained through 1975. A statistically significant increased risk of leukemia (7 observed, 1.48 expected; $p < .002$) was found by comparison of observed leukemia deaths in this cohort with those expected based upon general U.S. population death rates. The risk of leukemia was said by the authors to be potentially understated since follow-up was only 75% complete. According to the authors, there was no evidence of solvent exposure other than benzene. No effort was made to evaluate individual exposures to benzene for the purpose of doing a dose-response analysis. The main criticism of this study, as well as its later updates, is the small size of the cohort.
- In an extension and elaboration of the analysis done by Infante et al. (1977b), Rinsky et al. (1981) reported seven deaths from leukemia in this same cohort after achieving a 98% vital status ascertainment through June 1975. Forty additional deaths from all causes were reported, but no new leukemia deaths. Again, the risk of death from leukemia was statistically significant (standardized mortality ratio [SMR] was 560 based upon 7 leukemia deaths, $p < .001$). Some 437 members of the cohort were exposed for less than 1 year. Those who received 5 or more years of exposure exhibited an SMR of 2100, based upon 5 leukemia deaths versus 0.25 expected ($p < .01$). All seven leukemia cases were of the myelogenous or monocytic cell type. Four additional deaths from leukemia were also noted but could not be added to the total because they did not fit the criteria for inclusion. The authors tried to reconstruct past exposure to benzene at the two locations of this company and found that in some areas of the plants airborne benzene concentrations occasionally rose to several hundred parts per million, but most often employee 8-hour time-weighted averages (TWA) fell within the limits considered permissible at the time of exposure. No dose-response analysis was attempted.
- In an updated version of the Rinsky et al. (1981) study, the same authors examined a somewhat expanded cohort of 1165 non-salaried white men employed in the rubber hydrochloride department for at least 1 day through December 1965 and followed to December 31, 1981 (Rinsky et al., 1987). Follow-up was 98.6% complete. Again, a statistically significant excess risk of leukemia was found for the total cohort (9 observed, 2.7 expected; $p < 0.05$). For the first time, individual measurements of cumulative exposure in terms of ppm-years were generated for all members of the cohort utilizing the historical air-sampling data discussed above or interpolating estimates based on the existing data. SMRs for leukemia ranged from a non-significant 109 (2 observed, 1.83 expected) at cumulative exposures under 40 ppm-years to a statistically significant SMR of 2339 (5 observed, 0.21 expected; $p < .05$) at 200 ppm-years or more of exposure. The authors found significantly elevated risks of leukemia at cumulative exposures less than the then equivalent current standard for occupational exposure, which was 10 ppm over a 40-year working lifetime.

[redacted]

- The Rinsky et al. (1981, 1987) study analyses, based upon the original cohort of Pliofilm rubber workers studied by Infante et al. (1977b), were selected by the Agency as the critical study for dose-response analysis and for the quantitative estimation of cancer risk to humans. The Rinsky et al. (1981, 1987) analyses show ample power, latency, reasonably good estimates of exposure to benzene except prior to 1946, few confounders, and a wide range of exposure to benzene from low levels to high levels. Limitations include the small cohort size, reporting only nine leukemia deaths with no estimates of risk according to cell type. There remain questions about the estimation of personal exposure to benzene, especially prior to 1946 when no measurements of airborne benzene were made. And finally, at levels less than 200 ppm-years it is not possible to determine leukemia risk in this cohort because of lack of sensitivity of the data at low levels.

F.2.25 Benzo(a)pyrene, CASRN 50-32-8



Tier 3 Representative Aromatic

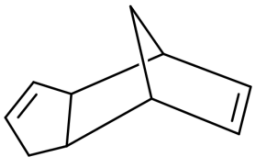
IRIS**:**

- Test Guideline Not Specified: Subchronic oral toxicity study in rats. Rats were treated with the test substance via oral gavage for 35 days. No other details provided. Immunological RfD = $2x10^{-3}$ mg/kg-d based on decreased thymus weight and serum IgM. (De Jon et al. 1999 and Kroese et al. 2001)
- Test Guideline Not Specified: Neurodevelopmental gavage study in rats. Rats were treated with the test substance via oral gavage on PND 5-11. No other details provided. Developmental RfD = $3x10^{-4}$ mg/kg-d based on neurobehavioral changes. (Chen et al. 2012. Principal study for Oral RfD)
- Test Guideline Not Specified: Subchronic reproductive toxicity study in rats. Rats were treated with the test substance via oral gavage for 60 days. No other details provided. Reproductive RfD = $4x10^{-4}$ based on decreased ovarian follicles and ovary weight observed. (Xu et al. 2010)
- Test Guideline Not Specified: Developmental inhalation study in rats. Rats were exposed to the test substance via inhalation on GD 11-20. Decreased embryo/fetal survival (i.e., increased resorptions) was observed. No other details provided. LOAEL = 25 µg/m^3 based on decreased embryo/fetal survival. Developmental RfC = $2x10^{-6}$ based on decreased embryo/fetal survival. (Archibong et al. 2002, Selected for derivation of RfC)
- Test Guideline Not Specified: Premating study in rats. Rats were exposed to the test substance via inhalation for 14 days. No other details provided. RfC = $3x10^{-6}$ mg/m3 based on reduced ovulation rate and ovary weight. (Archibong et al. 2012)
- Carcinogenic in humans.

[redacted]

- Test Guideline Not Specified: Carcinogenicity bioassay in mice. B6C3F1 mice were administered the test substance via the oral route. No other details provided. OSF = 1 mg/m^3 based on tumor response in the alimentary tract (forestomach, esophagus, tongue, and larynx). (Beland and Culp, 1998)
- Test Guideline Not Specified: Carcinogenicity bioassay in hamsters. Male Syrian Golden hamsters were exposed via inhalation to benzo[a]pyrene condensed onto sodium chloride particles for 130 weeks. No other details provided. IUR = 6×10^{-4} per ug/m3 based on the occurrence of upper respiratory and upper digestive tract (forestomach) tumors in males. Calculated from a $BMCL_{10}$ of 0.16 mg/m^3. (Thyssen et al., 1981.)

F.2.26 Dicyclopentadiene, CASRN 77-73-6



Tier 3 Representative Olefin

Health Canada (2019) Draft Screening Assessment for Dicyclopentadiene (Excerpted):

"A NOAEL from an oral study was used to characterize the risk for per event dermal exposure to DCPD, as there was no dermal toxicity study. There are 13-week inhalation studies with DCPD available, which are considered a more appropriate route of exposure for comparison with inhalation exposure scenarios. In addition, the oral study was not used for the per event inhalation scenarios because effects in the kidneys (hyaline droplets, basophilic change of the tubular epithelium, increased absolute and relative kidney weights) and adrenal gland effects (an increase of fatty droplets in the fascicular zone) observed after 44 days exposure with 20 mg/kg bw/day DCPD by gavage (equivalent to 64.5 mg/m^3 6) in male rats (MHW 1997) were either not observed (adrenal effects, some of the kidney effects) at the 2-week interim sacrifice in the 13-week inhalation study in rats or were reversible (hyaline droplet formation) at higher doses (up to 275 mg/m^3) in the 13-week inhalation study in rats (Dodd et al. 1982 in OECD 2002a). As such, use of this oral study is considered overly conservative for comparison to the inhalation exposure scenario."

"A combined repeated-dose and reproductive/developmental toxicity screening test was conducted in SD rats (MHW 1997 in OECD 2002a). Test animals were administered 0, 4, 20, or 100 mg/kg bw/day DCPD in olive oil (10/sex/dose) by gavage for 44 days in males and from 14 days prior to mating to day 4 of lactation (approximately 38 days) for females. At 4 mg/kg bw/day and above, an increase in hyaline droplets in the tubular epithelium of the kidney was observed in all males (MHW 1997). At 20 mg/kg bw/day and above there were other kidney effects (basophilic change of the tubular epithelium, increased absolute and relative kidney weights) and adrenal gland effects (an increase of fatty droplets in the fascicular zone) in males. At 100 mg/kg bw/day, there were also liver effects in males (single cell necrosis, increased absolute and relative liver weights, clinical chemistry changes) and

[redacted]

effects in the adrenal glands (increase of fatty droplets in the fascicular zone) in a female. In addition, two females in the 100 mg/kg bw/day group died prior to pregnancy (necropsy indicated lung congestion, adrenal gland enlargement, thymic bleeding and gastric mucosal surface bleeding). At 100 mg/kg bw/day, two dams lost all neonates within two days (OECD 2002a). It was unclear whether this was due to a lack of nursing and/or matricide (MHW 1997, OECD 2002a, ECHA c2007-2019). This resulted in a decreased pup viability index on postnatal day (PND) 4 at 100 mg/kg bw/day. Pups in the 100 mg/kg bw/day group also had lower body weights (PNDs 0 and 4) and body weight gains (PND 0 to 4) relative to control pups (MHW 1997, ECHA c2007-2019). The OECD (2002a) reported no observed effect levels (NOELs) for males/females of 4/20 mg/kg bw/day [repeated-dose toxicity], 100/20 mg/kg bw/day [reproductive toxicity], and 100 mg/kg bw/day [offspring toxicity]. In this assessment the parental no observed adverse effect level (NOAEL) for males was considered to be 4 mg/kg bw/day based on the kidney and adrenal gland effects in males at the lowest adverse effect level (LOAEL) of 20 mg/kg bw/day."

EPA PPRTV (2014):

Oral Study used for POD derivation in PPRTV:

One-generation reproductive study in minks. PPRTV summary: Aulerich et al. (1979) is selected as the principal study for the derivation of the subchronic and chronic p-RfDs. This report is not peer-reviewed but was evaluated by IRIS for the assessment of DIMP (U.S. EPA, 1993). In this one-generation reproductive study, 30 (6 males and 24 females per dose group), 3-month old, dark variety minks were administered 0-, 100-, 200-, 400-, or 800-ppm (estimated as 0, 23.6, 42.4, 85.0, or 169.9 mg/kg-day for combined male and female minks by the study authors through measured food consumption and body-weight data; see Table B.16) DCPD (purity >99%) in the diet for 12 months, equivalent to one reproductive season. The life span of a mink in captivity has been estimated to be up to 8 years (Basu, 2013); therefore, this 12-month reproductive study represents a chronic exposure duration for the F0 animals as the treatment with DCPD occurred for greater than 10% of the total mink life span. Mortality and other signs of toxic stress were recorded throughout the duration of the experiment, although the frequency was not recorded. Body weight and feed consumption were measured every 2 weeks, with the exception of the gestation period. Blood samples (for packed cell volume and hemoglobin) and blood smears (for differential leukocyte counts) were collected prior to the study initiation, at 3-month intervals through the study, and at the conclusion of the study. All parameters were evaluated utilizing analysis of variance and Dunnett's t-test. The authors did not report GLP compliance status.

Mating began on March 1, 1978, and continued for approximately 20 days, during which females were introduced into the males' cages every fourth day for up to an hour (or until a positive mating confirmation was made). Whenever possible, mating pairs in the same treatment group were used. After successful breeding, the females were transferred to individual cages with a nest box and provided with shredded wood, used for both insulation and nesting material during whelping. During whelping (April 20−May 15), the nest boxes

[redacted]

were checked daily for evidence of kits; when found, newborn kits were sexed, and both mother and kit were weighed at whelping and when kits were 1 month of age. Gestation length, litter size, sex ratio, kit mortality, increase in kit biomass during lactation, and changes in the weight of the lactating female were recorded. At study termination, all minks were weighed, blood samples collected via cardiac puncture, and the animals sacrificed. The following whole organs were removed during necropsy, weighed, and evaluated for pathomorphological changes: brain, liver, kidneys, spleen, gonads, lungs, heart, and adrenal glands as well as portions of the intestine, stomach, skeletal muscle, adipose tissue, and integument.

Chronic ingestion of DCPD in the diet of minks at concentrations up to 169.9 mg/kg-day for 12 months did not result in treatment-related mortality in any of the groups (Aulerich et al., 1979). Changes in body weight showed no dose-related trend, although in a few instances, animals in the highest exposure group (169.9 mg/kg-day) were reported to have reduced body weights compared to the control animals; however, when analyzed as a change in body-weight percentage over the course of compound administration, these changes were not apparent (see Table B.17). Feed consumption in the high dose group was initially reduced compared to controls but was reported as greater than controls by study termination (although this change was not reported as statistically significant). Changes in hematological values (including packed cell volume, hemoglobin, and differential leukocyte counts) were equally inconsistent and not found to be dose dependent.

No treatment-related effects on reproductive performance were reported in male or female minks following exposure to DCPD. Whelping rates, gestation length, fecundity, kit weight at birth, and secondary sex ratios were also unaffected. Although kit mortality was not altered by DCPD, the absolute weight of kits during lactation was statistically significantly depressed at Week 4 for animals in the 42.4-, 85.0-, or 169.9-mg/kg-day treatment groups (see Table B.18). The study authors hypothesized that the reduced absolute weight was attributable to either a toxicological effect on the kits through direct ingestion of the chemical in milk or indirectly through a perturbation in maternal metabolism, which affected lactation. When the organs were evaluated following study termination, the only statistically significant changes reported between the treatment and control samples were a reduction in spleen weight in the 85.0-mg/kg-day group (2.4 ± 0.16 vs. 3.3 ± 0.29 g, respectively) and a reduction in the weight of the testes in the 169.9-mg/kg-day group (1.1 ± 0.1 vs. 1.8 ± 0.1 g, respectively; see Table B.19). Although a reduction in spleen weight was reported at 85.0 mg/kg-day, this effect was not observed in the highest dose group, and therefore, the study authors explained the reduction as occurring from chance variation or sampling error. Likewise, the study authors explained the reduction in testes weight observed in the high dose group as the normal seasonal reduction that occurs in this species.

[redacted]

The study authors concluded that chronic ingestion of DCPD in the diet of minks had no adverse effect on growth, survival, or reproductive performance. However, the absolute weight of neonates from lactating dams fed 42.4-, 85.0-, or 169.9 mg/kg day DCPD was statistically decreased in a dose-dependent manner compared to that of neonates for dams in the control or low-dose group. Spleen weight was reduced at 85.0 mg/kg-day, and testes weight was reduced at 169.9 mg/kg-day, respectively, but the study authors did not consider these reductions to be treatment related. No NOAEL or LOAEL was reported in the study, but based on reductions in the kit weight following 4 weeks of nursing at the three highest concentrations, a LOAEL of 42.4 mg/kg-day and a NOAEL of 23.6 mg/kg-day are identified.

Key Inhalation Study:

- 90-day inhalation study in rats. PPRTV summary: Exxon (1980) is selected as the principal study for the derivation of the screening subchronic and chronic p-RfCs. In a non-peer-reviewed subchronic-duration (90-day) inhalation study performed by Exxon (1980) and reported in Dodd et al. (1982), Fischer 344 (F344) rats (51 male and 51 female rats per exposure concentration) were exposed to target concentrations of 0-, 1-, 5-, or 50-ppm in air; actual air concentrations were 0-, 1.0-, 5.1-, or 51.0-ppm DCPD (purity 95%) for 6 hours/day, 5 days/week, for 13 weeks. The corresponding HECs are calculated as 0, 0.97, 4.9, and 49 mg/m^3. Nine animals/sex/concentration were sacrificed at Weeks 3, 7, 14, 18, and 27 of the study, with Weeks 18 and 27 corresponding to Weeks 4 and 13 postexposure. These sacrifice periods were identified as Groups A, B, C, D, and E, respectively, throughout the remainder of the study report.

  All animals were weighed the morning before the first exposure (reference weight), and this value was subtracted from each subsequent weight measurement to obtain the change in body weight throughout the course of the experiment. Body-weight measurements were taken weekly for the first 4 weeks and then every 2 weeks for the remainder of the exposure. The animals' weights were collected again prior to sacrifice. Mean food (see Table B.20) and water consumption (see Table B.21) were measured during urine collection periods and standardized to 24-hour rates (Group B rats only), allowing comparisons to be made between measurement periods for each exposure group. Each animal also underwent an ophthalmologic examination (prior to sacrifice interval). Other tests included blood chemistry (prior to sacrifice interval), histopathology of kidneys and urinary bladder following necropsy, and electron microscopy of kidney tissue at the sacrifice intervals at Weeks 14 and 17. Additionally, upon sacrifice, a necropsy of the animal was performed, and the following organs removed and weighed: kidney (left and right, weighed individually), lung, liver, and testes (males). The study authors did not report GLP compliance status.

  One male rat died accidently following the 16th exposure (reason not reported); no other rat mortality was observed in the study. Observation of the rats during the 6-hour

exposure period indicated normal appearance of all rats. Several conditions recorded in the exposure groups were also recorded in the control group including urogenital area wetness (females), lacrimation, and alopecia (males). However, during the recovery period, these observations were recorded only in exposed rats, not in control rats. No statistically significant changes in body weight occurred in either the control or exposed rats throughout the study duration. Changes in food consumption results were observed in male and female rats; however, the differences were not related to the DCPD concentration or the number of exposures. A decrease in food consumption was reported at 92 days postexposure in all DCPD exposure groups and was accompanied by a depression in body weight at the 4.9-mg/m^3 concentration level. However, the biological significance of these findings was not assessed by the study authors.

Although concentration-related differences were observed with respect to blood analysis, they were not found to be biologically significant. The following differences were observed: hematology (e.g., depression in red blood cells of male rats at the highest exposure concentration), serum chemistry (e.g., an increase in serum calcium and a decrease in alanine aminotransferase in males exposed to 4.9 and 49 mg/m^3 DCPD), and the ophthalmologic examination (mild conjunctivitis with lacrimation in the eyes of male rats at both 4.9 and 49 mg/m^3 in Group B; a nonreactive dilated pupil was observed in one control [Group C] and one 49-mg/m^3 female rat [Group D]; and two female rats exposed to 0.97 and one to 4.9 mg/m^3 developed conjunctivitis with lacrimation in Group E).

The urinalysis results showed that the majority of male rats exposed to 49 mg/m^3 and many of the rats exposed to 4.9 mg/m^3 DCPD had a decrease in urine specific gravity and osmolality, which was concentration dependent and related to the number of DCPD exposures and the concentration of DCPD (see Table B.22). Analysis of the urinary sediment content in male rats showed evidence of toxic renal damage, with epithelial cells and epithelial cell casts being found in rats from 8 completed exposures and after as much as 29 days of recovery (see Table B.22). The presence of the epithelial cells and casts was reported as dependent on the DCPD concentration. Trends in urinary excretion rates were also reported, including a statistically significant decrease in calcium and sodium and an increase in potassium in the latter part of the exposure regimen (in the 49-mg/m^3 group; a similar trend was observed in the 4.9-mg/m^3 group, although the values were not statistically significant). It is important to note that these findings were solely identified in males, as no abnormal urinary findings were reported in female rats.

The results of the gross necropsy showed an increased incidence of tubular hyperplasia and a reticular pattern in the kidneys of males exposed to 49-mg/m^3 DCPD. A similar reticular pattern, accompanied by a generalized color change of the kidney, was observed in Group A male rats exposed to 4.9 and 49 mg/m^3 DCPD at an earlier sacrifice

period. The study authors reported no statistically significant differences in the gross lesions between exposed and control groups and that these effects were reversible and no longer apparent at the end of the exposure regimen or at recovery sacrifice. Organ weights followed a similar pattern, with a statistically significant increase in relative liver weights in male rats exposed to the highest concentration of DCPD (Groups A, B, and C). However, the increases at 49 mg/m^3 were not greater than 10% over controls (9.9, 4.8, and 6.9 in the A, B, and C groups, respectively). Although male rats exposed to 0.97 mg/m^3 also exhibited increased absolute liver weights, the body weights of the animals exposed to 0.97 mg/m^3 were greater than the body weights of control animals, so changes in relative liver weight were minimal. A statistically significant increase in both relative and absolute kidney weight for the left and/or right kidney was also found in male rats from Groups A, B, and C exposed to 49 mg/m^3 when compared to controls. However, these differences were not consistently greater than 10% for all three groups, were reversible [not observed by postexposure Day 29 (see Table B.23)]. Group E female rats exposed to 0.97- and 49-mg/m^3 DCPD had a statistically significant decrease in the relative weight of the left kidney only. Due to these decreases being slight and not observed in the right kidney, Exxon (1980) and Dodd (1982) attributed the observation to body-weight gain throughout the course of the experiment. No other instances of organ-weight differences were reported among DCPD-exposed female rats.

Exxon (1980) and Dodd (1982) hypothesized that the kidney lesions, which progressively worsened throughout the exposure and recovery phase of the study, were due to chronic glomerulonephrosis, a common syndrome in F344 rats. This syndrome occurs in conjunction with advancing age in both male and female rats. However, the presence of epithelial cells and casts, regenerative epithelium (tubular hyperplasia), and dilation of the tubule in the kidneys, coupled with the most severe effects being observed in male species, could be indicative of an alpha 2u-globulin pathway. Although staining for hyaline droplets was not reported by Exxon (1980) or Dodd (1982), Bevan et al. (1992) used data from Exxon (1980) to examine hyaline droplets and quantify severity indices. The histological examination of the kidneys from rats exposed to 4.9 and 49 mg/m^3 by Bevan et al. (1992) showed the formation of hyaline droplets in the proximal convoluted tubules at a much greater level than the control rats (see Table B.24). The formation of these droplets was concentration dependent in nature and later confirmed through electron microscopy. By Week 13 of exposure, male rats exposed to 49 mg/m^3 DCPD developed tubular proteinosis, which persisted after the recovery period. Similar results were observed in the regenerative epithelium, which increased in severity throughout the exposure (see Table B.25) and lessened only minimally throughout the recovery. No liver or kidney changes were observed or reported in female rats. A study by Hamamura et al. (2006), which performed immunohistochemical analysis, suggests that hyaline droplets forming in male rats following DCPD exposure are composed of alpha 2u-globulin. However, the Hamamura et al. (2006) study was short term, exposed animals only through the oral route, and utilized a small sample size. Additionally, the subchronic-duration oral rat study by Hart (1976) utilized a larger sample size and higher

[redacted]

DCPD concentrations than Hamamura et al. (2006) but did not report any kidney effects. Taken together, these data suggest that the relevance of the rat kidney lesions observed in the Exxon (1980) study to humans cannot be discounted. Hence, the increased formation of hyaline droplets in the kidneys of male rats is considered the critical effect, with a LOAEL of 4.9 mg/m^3 and a NOAEL of 0.97 mg/m^3. No biologically significant toxicity was observed in female rats at any concentration tested (NOAEL of 49 mg/m^3, the highest concentration tested).

F.2.27 n-Nonane, CASRN 111-84-2

Tier 3 Representative Paraffin

OECD SIDS

- NON-GUIDELINE STUDY, comparable to OECD 403: LC50 (rat)(4-hr) = 17000 mg/m^3 (3200 ppm)
- NON-GUIDELINE STUDY, comparable to OECD 403: LC50 (rat)(8-hr) = 23,733 mg/m^3 (4467 ppm)
- Test Guideline Not Specified: Moderately irritating in rats; scored by Draize method
- NON-GUIDELINE STUDY, comparable to OECD 471: Ames Assay. Negative in Salmonella with and without metabolic activation
- NON-GUIDELINE STUDY, comparable to OECD 408: 90-day oral toxicity study in rats and mice. Female Fischer 344 rats (10/group) and male C57Cl/6 mice (10/group) were administered the test substance via oral gavage at doses of 0, 100, 1000, or 5000 mg/kg/day for 7 days/week, 90 days. SIDS reported NOAEL = 100 mg/kg/day and LOAEL = 1000 mg/kg/day based on histopathological lesions (hyperplasia and hyperkeratosis with mild inflammation and multifocal minimal to mild necrosis in the alimentary tract; suppurative inflammation of nasal turbinates; in rats only, pulmonary effects consistent with aspiration of foreign material).
- NON-GUIDELINE STUDY, comparable to OECD 413: Subchronic inhalation toxicity study in rats. Male Albino Harlan-Wistar rats (25/group) were exposed to the test substance (purity=98.4%) via whole body inhalation at concentrations of 0, 1888, 3095, or 8393 mg/m^3 (~360, 590, 1600 ppm) for 6 hours/day, 5 days/week, over 13 weeks for a total of 63 exposures. NOAEC = 3095 mg/m^3 and LOAEC = 8393 mg/m^3 (590 ppm) based on weight changes and clinical signs (salivation, mild loss of coordination, fine tremors, lacrimation) at the high-dose.

PPRTV (EPA 2009g)

- Non-guideline study, comparable to OECD 403: LC50 (rat)(4-hr) = 17000 mg/m^3 (3200 ppm)
- Non-guideline study, comparable to OECD 403: LC50 (rat)(8-hr) = 23,733 mg/m^3 (4467 ppm)

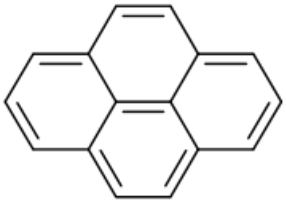
[redacted]

- Non-guideline study, comparable to OECD 471: Ames Assay. Negative in Salmonella with and without metabolic activation
- Non-guideline study, comparable to OECD 408: 90-day oral toxicity study in rats and mice. Female Fischer 344 rats (10/group) and male C57CI/6 mice (10/group) were administered the test substance via oral gavage at doses of 0, 100, 1000, or 5000 mg/kg/day for 7 days/week, 90 days. PRTV reported LOAEL = 100 mg/kg/day based on the lesions observed in the forestomach of rats and mice at all doses. No NOAEL.
- Test guideline not specified: 7-day range finding study in rats and mice. Female Fischer 344 rats (5/group) and male C57CI/6 mice (5/group) were administered the neat test substance via oral gavage at doses of 0, 700, 1800, or 3600 mg/kg/day for 7 days. NO POD established. Neurobehavioral tests were inconclusive. Increased liver weights in mice ≥1800 mg/kg/day and increased spleen weights at 3600 mg/kg/day. In rats, decreased body weights at 3600 mg/kg/day.
- Non-guideline study, comparable to OECD 413: Subchronic inhalation toxicity study in rats. Male Albino Harlan-Wistar rats (25/group) were exposed to the test substance (purity=98.4%) via whole body inhalation at concentrations of 0, 1888, 3095, or 8393 mg/m^3 (~360, 590, 1600 ppm) for 6 hours/day, 5 days/week, over 13 weeks for a total of 63 exposures. NOAEC = 3095 mg/m^3 and LOAEC = 8393 mg/m^3 (590 ppm) based on weight changes and clinical signs (salivation, mild loss of coordination, fine tremors, lacrimation) at the high-dose.
- Test guideline not specified: Short-term repeated dose study in rats. Female Harlan-Wistar rats (10/group) were exposed to the test substance at a concentration of 12000 mg/m^3 for 2 consecutive days. No POD. Within 3-hrs, poor coordination, tremors, and clonic spasms observed.
- Test guideline not specified: Short-term repeated dose study in rats. Female Harlan-Wistar rats (10/group) were exposed to the test substance at a concentration of 10000 mg/m^3 for 6 hours/day, 3 consecutive days. After a period of rest (one weekend), rats were exposed for an additional 4 days. No POD. Minor coordination loss, mild tremors, ad slight irritation of the eyes and extremities observed.

NTP

- NTP Protocol: Ames Test. Negative in Salmonella with and without metabolic activation

F.2.28 Pyrene, CASRN 129-00-0



Tier 3 Representative Aromatic

[redacted]

PPRTV for Pyrene (2007)

- Test Guideline Not Specified: 13-week oral gavage study in CD-1 mice (20/sex/dose) at doses of 0, 75, 125, or 250 mg/kg/day in corn oil. NOAEL = 75 mg/kg/day and LOAEL = 125 mg/kg/day based on nephropathy (multiple foci of renal tubular regeneration, interstitial lymphocytic infiltrates, foci of interstitial fibrosis) and decreased kidney weights. IRIS RfD = 0.25 mg/kg/day or 3E-2 mg/kg/day

[redacted]

Appendix G: Petroleum Constituent PODs Considered for Assessment

Table G-1. Petroleum Constituent Inhalation PODs Considered for Assessment of Waste Plastics

Name	CASRN	# of Carbons	PIONA Class	POD type	Adjusted POD (mg/m^3)	Study Type	Hazard Endpoint	Reference
Benzo[a]pyrene	50-32-8	20	A	LOAEC	0.0042	Inhalation	Decreased embryo/fetal survival	Archibong et al. (2002) as cited in EPA (2017)
1-Methyl naphthalene	90-12-0	11	A	LOAEC	0.54	13 week rat inhalation study	Mucous cell hyperplasia in nasopharyngeal tissues of males	Kim et al. (2020)
2-Methyl naphthalene	91-57-6	11	A	NOAEC	0.36	4 week inhalation study in rats	Histopathology changes in lungs (mononuclear cell infiltration, proteolysis, increased goblet cell numbers) and liver (bile duct hyperplasia)	Świercz et al. (2011)
Dicyclopentadiene	77-73-6	10	O	NOAEC	0.97	Subchronic rat inhalation study	Increased hyaline droplets in proximal convoluted tubules in male rat kidneys	Exxon Chemical Company (1980); Dodd et al. (1982); Bevan et al. (1992) as cited in EPA (2014)
Benzene	71-43-2	6	A	$BMCL_{1SD}$	8.2	Subchronic occupational study	Decreased lymphocyte count	Rothman et al. (1996) as cited in EPA (2003a) IRIS and EPA (2009a)
1,2,4-Trimethyl benzene	95-63-6	9	A	BMCL	25.1	Subchronic rat inhalation neurotoxicity study	Decreased pain sensitivity in rats exposed to 1,2,4-TMB	Korsak and Rydzynski (1996) as cited in EPA (2016a)
1,1-Biphenyl	92-52-4	12	A	$BMCL_{10}$	32.8	Inhalation	Congestion and edema in the liver and kidneys	Cannon Laboratories Inc. (1977) as cited in EPA (2011a)
n-Nonane	111-84-2	9	P	NOAEC	554	Subchronic rat inhalation study	Consistent suppression of weight gain and clinical signs at 8,400 mg/m3	Carpenter et al. (1978) as cited in OECD (2010a)

[redacted]

Table G-1. Petroleum Constituent Inhalation PODs Considered for Assessment of Waste Plastics

Name	CASRN	# of Carbons	PIONA Class	POD type	Adjusted POD (mg/m^3)	Study Type	Hazard Endpoint	Reference
2-Methyl propene	115-11-7	4	O	NOAEC	819	Combined Chronic Toxicity/Carcinogenicity Study	Hyaline degeneration of olfactory epithelium and hypertrophy of goblet cells lining the nasopharyngeal duct	NTP (1998) as cited in OECD (2004b)
2-Methyl pentane	107-83-5	6	I	**LOAEC**	1420	Subchronic rat inhalation neurotoxicity study	Decreased body weight gain; No effects on hindlimb spread or tibial nerve histology	Frontali et al. (1981)

[redacted]

Table G-2. Petroleum Constituent Oral PODs Considered for Assessment of Waste Plastics

Chemical Name	CASRN	# of Carbons	PIONA Class	POD type	Adjusted POD (mg/kg/day)	Study Type	Hazard Endpoint	Reference
Benzo[a]pyrene	50-32-8	20	A	$BMDL_{1SD}$	0.092	Neurodevelop-mental study in rats	Neurobehavioral changes	Chen et al. (2012) as cited in EPA (2017)
Benzene	71-43-2	6	A	BMDL	1.2	RTR extrapolation	Decreased lymphocyte count	Rothman et al. (1996) as cited in EPA (2003a) and EPA (2009a)
n-nonane	111-84-2	9	P	BMDL	3.13	90 day mouse study	Proliferative forestomach lesions	Dodd et al. (2003) as cited in EPA (2009g)
1,2,4-Trimethyl benzene	95-63-6	9	A	$BMDL_{HED}$	3.5	RTR via PBPK	Decreased pain sensitivity in rats exposed to 1,2,4-TMB	Korsak and Rydzynski (1996) as cited in U.S. EPA (2016a)
2-Methyl naphthalene	91-57-6	11	A	$BMDL_{05}$	3.5	81 week diet study in mice	Pulmonary alveolar proteinosis	Murata et al. (1997) as cited in EPA (2007a)
Dicyclopenta diene	77-73-6	10	O	NOAEL	4	Oral combined repeat dose and developmental/ reproductive screening	Kidney and adrenal effects in males	MHW (1997a) as cited in Health Canada (2019)
1-Methyl naphthalene	90-12-0	11	A	LOAEL	71.6	81 week diet study in mice	Pulmonary alveolar proteinosis	Murata et al. (1993) as cited in EPA (2008a)
1,1-Biphenyl	92-52-4	12	A	$BMDL_{05}$	9.59	Developmental toxicity study	Fetal skeletal anomalies	Khera et al. (1979) as cited in EPA (2011a)
1-Methyl naphthalene	90-12-0	11	A	NOAEL	50	Oral combined repeat dose and developmental/ reproductive screening	Increased liver weight in males and females; increased kidney weight in males	METI (2009)
1,1-Biphenyl	92-52-4	12	A	$BMDL_{10}$	58	2 year diet study	Renal papillary mineralization in male rats	Umeda et al. (2002) as cited in U.S. EPA (2013)
Pyrene	129-00-0	16	A	NOAEL	75	90-day oral mouse study	Nephropathy and decreased kidney weights	EPA (1989a) as cited in EPA (1990a) and EPA (2007b)
2-Methyl	107-83-5	6	I	LOAEL	1000	4-8 week rat oral	Slightly decreased distal	Ono et al. (1981)

[redacted]

Table G-2. Petroleum Constituent Oral PODs Considered for Assessment of Waste Plastics

Chemical Name	CASRN	# of Carbons	PIONA Class	POD type	Adjusted POD (mg/kg/day)	Study Type	Hazard Endpoint	Reference
pentane						neurotoxicity study	and proximal mixed nerve conduction velocity	
1,3-Pentadiene	504-60-9	5	O	NOEL	100	Oral combined repeat dose and developmental/ reproductive screening	Transient decrease in food consumption in maternal animals at 1000 mg/kg/day; no adverse reproductive/development al effects at highest dose on P or F1 generations	Exxon Biochemical Sciences, Inc. (1992) as cited in OECD (1994)
2-Methyl propene	115-11-7	4	O	NOAEL	148.6	28-Day Repeated Dose Oral Toxicity in Rodents	No adverse effects	Hazleton (1986) as cited in OECD (2004b)

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Appendix H: Exposure Limit Calculations

New Chemical Exposure Limit (NCEL) for Occupational Inhalation Exposures

Case	POD Basis (Tier)	POD	Blood:Air Partition Coefficient ratio (animal/ human)	POD Exposure duration (hours/day)	POD Exposure Frequency (days/week)	Uncertainty Factor	NCEL, 8 h Time-weighted Average (mg/m3)
P-21-0144	Tier 3	0.97	1	24	7	100	0.021
P-21-0146	Tier 3	3	1	6	5	1000	0.00117
P-21-0148	Tier 2 (POD 1)	2200	1	6	7	100	12
	Tier 2 (POD 2)	2300	1	6	5	100	9.0
	Tier 3	0.97	1	24	7	100	0.021
P-21-0152	Tier 3	0.025	1	4	7	1000	0.0000091
P-21-0154	Tier 3	0.025	1	4	7	1000	0.0000091

Drinking Water Equivalent Level ($DWEL_{TSCA}$) for General Population Oral Exposures via Drinking Water

Case	POD Basis	POD	Benchmark MOE	Adult DWEL mg/l (ppm)	Infant DWEL mg/l (ppm)
P-21-0144	Tier 3	3.5	100	1	0.23
P-21-0148	Tier 2 (POD 1)	500	100	132	33
	Tier 2 (POD 2)	500	1000	13	3.3
	Tier 3	1.2	10	3	0.79
P-21-0149	Tier 2	500	1000	13	3
P-21-0150	Tier 3	3.13	100	0.83	0.21
P-21-0152	Tier 3	0.092	100	0.02	0.01
P-21-0157	Tier 3	3.5	100	0.92	0.23

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Fish Ingestion Exposure Limit (FIEL) for General Population Fish Ingestion

Case	POD Basis	POD	Benchmark MOE	% of PMN	BCF	FIEL (ppb)
P-21-0144	Tier 2	500	1000	100	7892	20
	Tier 3	3.5	100	60	7892	2.1
P-21-0145	Tier 2	500	1000	100	33,260	4.3
	Tier 3	3.13	100	3	33,260	8.99
P-21-0148	Tier 2 (POD 1)	500	100	100	1023	1400
	Tier 2 (POD 2)	500	1000	100	1023	140
	Tier 3	1.2	10	22	1023	150
P-21-0149	Tier 2	500	1000	100	1213	120
	Tier 3	1000	1000	44.52	1213	530
P-21-0150	Tier 3	3.13	100	100	2014	4.5
	Tier 3	3.13	100	11	2014	40
P-21-0152	Tier 3	0.092	100	100	3.2	82.44
	Tier 3	0.092	100	93	3.2	88.64
P-21-0155	Tier 3	3.5	100	100	808,000	0.0124
	Tier 3	3.5	100	77	808,000	0.016
P-21-0156	Tier 3	3.5	100	100	808,000	0.012
	Tier 3	3.5	100	60	808,000	0.021
P-21-0157	Tier 3	3.5	100	100	1,690,000	0.00594
	Tier 3	3.5	100	21	1,690,000	0.0283
P-21-0158	Tier 2	500	1000	100	4,710,000	0.0304
	Tier 3	305	100	9	4,710,000	0.0237

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Appendix I: Acronyms and Abbreviations

A = aromatics
ACR = acute:chronic ratio
ADD = average daily dose
ADR = acute dose rate
AEGL = Acute Exposure Guideline Level
ALD = Approximate Lethal Dose
API = American Petroleum Institute
ATSDR = Agency for Toxic Substances and Disease Registry
BAF = bioaccumulation factor
BCF = bioconcentration factor
Benchmark MOE = benchmark margin of exposure typically considered to be an acceptable amount of exposure and not constitute a risk
BMCL = benchmark concentration lower confidence limit
$BMCL_{1SD}$ = benchmark concentration lower confidence limit using 1 standard deviation from control mean as benchmark response
BMDL = benchmark dose lower confidence limit
$BMDL_{1SD}$ = benchmark dose lower confidence limit using 1 standard deviation from control mean as benchmark response
BP = boiling point
bw = body weight
C = carbon number
CASRN = chemical abstracts service registry number
CHL = Chinese hamster lung
CHO = Chinese hamster ovary
ChV = chronic value
CNS = central nervous system
COC = concentration of concern
d = day
Da = Daltons
DNA = Deoxyribonucleic acid
DW = drinking water
DWEL = drinking water equivalent level
EC_{50} = effective concentration for 50% of population
ECHA = European Chemicals Agency
EPI = EPI (Estimation Program Interface) Suite™
EU = European Union
F1 = first generation
F2 = second generation

[redacted]

FIEL = fish ingestion exposure limit
GC = gas chromatography
GD = gestation day
GHS = Globally Harmonized System
GI = gastrointestinal
h = hour
HC = US EPA Hazard Characterization
I = isoparaffins
i.p. = intraperitoneal
IRIS = Integrated Risk Information System
IUR = inhalation cancer unit risk
LADD = lifetime average daily dose
LAN-D = naphtha (petroleum), light alkylate distillate
LC_{100} = lethal concentration for 100% of population
LC_{50} = lethal concentration for 50% of population
LD = lactation day
LD_{50} = lethal dose for 50% of population
$LOAEC_{adj}$ = lowest observed adverse effect concentration adjusted for continuous-equivalent exposure (24 hours/day, 7 days/week)
LOAEL = lowest observed adverse effect level
$LOAEL_{adj}$ = lowest observed adverse effect level adjusted for continuous-equivalent exposure (24 hours/day, 7 days/week)
LOEC = lowest observed effect concentration
LOEL = lowest observed effect level
$LOEL_{adj}$ = lowest observed effect level adjusted for continuous-equivalent exposure (24 hours/day, 7 days/week)
Log K_{ow} = log octanol-water partition coefficient
Log P = log partition coefficient
MOE = margin of exposure
MP = melting point
MSDS (or SDS) = material safety data sheet
MW = molecular weight
N = Naphthenics
NCEL = New Chemical Exposure Limit
NCS = new chemical substance
NOAEC = no observed adverse effect concentration
$NOAEC_{adj}$ = no observed adverse effect concentration adjusted for continuous-equivalent exposure (24 hours/day, 7 days/week)
NOAEL = no observed adverse effect level
$NOAEL_{adj}$= lowest observed adverse effect level adjusted for continuous-equivalent exposure (24 hours/day, 7 days/week)

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NOEC = no observed effect concentration
NOEL = no observed effect level
$NOEL_{adj}$ = no observed effect level adjusted for continuous-equivalent exposure (24 hours/day, 7 days/week)
NTP = National Toxicology Program
O = olefins
OECD = Organisation for Economic Co-operation and Development
OPPTS = Office of Prevention, Pesticides and Toxic Substances
OSF = oral cancer slope factor
P = paraffins
PC = partition coefficient
PDD = permissible daily dose
PDR = potential dose rate
PIONA or P(I)ONA =Paraffin, Isoparaffin, Olefin, Naphthene, Aromatic
PMN = pre-manufacture notice
PND = postnatal day
POD = point of departure
PPRTV = Provisional Peer-Reviewed Toxicity Value
p-RfC = provisional reference concentration
p-RfD = provisional reference dose
QSAR = quantitative structure-activity relationship
RD_{50} = concentration leading to 50% depression in respiratory rate
RfC = reference concentration
RfD = reference dose
SD = Sprague-Dawley
s-H2O = water solubility
SIDS = Screening Information Data Set
TSCA = Toxic Substances Control Act
TWA = time weighted average
v/v = volume:volume ratio
VP = vapor pressure
wk = week
Wt % = weight:weight ratio